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Reaction of 3-azidoisoxazoles with active methylene compounds

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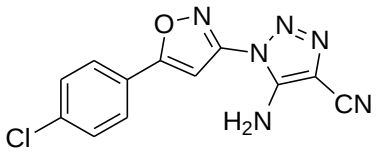
Experimental part

General details. Caution! Organic azides may cause damage and should be carefully handled. The maximum reaction scale was limited to 1.0 mmol. Temperatures above 35ºC are not recommended. Protective gear is needed with larger scales. Other useful recommendation for handling of azides can be found in source.[S1] Starting azidoizoxazoles were obtained by procedure described in our work.[S2]

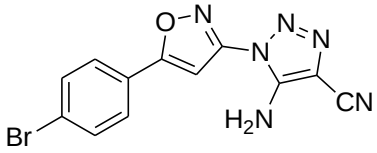
The NMR spectra were recorded on 400 MHz spectrometer at 400.1 MHz for ^{1}H NMR and at 100.6 MHz for ^{13}C NMR. Melting points were determined on glass capillary tubes. IR spectra were recorded on IR spectrometer with Fourier transform. Registration of IR-spectra was carried out at a resolution of 4 cm^{-1}, the number of scans 20. HRMS spectra were acquired at MicroTof Bruker Daltonics and Orbitrap Elite instrument using electrospray ionization (ESI).

General procedure for synthesis of compounds 2a-c, 3a-c and 4a,b. Sodium hydride (0.525 mmol, 21 mg of 60% dispersion in mineral oil) was carefully added to absolute ethanol (10 ml). To the resulted solution of sodium ethoxide, a solution of the corresponding methylene-active compound (0.525 mmol) in ethanol (1 ml) was added dropwise, and the resulted mixture was chilled to -20°C. After that a solution of appropriate azidoisoxazole **1** (0.5 mmol, 110 mg) in ethanol (5 ml) was added dropwise. The mixture was stirred for 30 min at -20°C and allowed to reach room temperature. Then it was acidified with acetic acid to pH 6 and warmed at 60°C for 2 h. After cooling, the precipitate was filtered off then rinsed with fresh ethanol and ether. The combined filtrates were concentrated and were worked up giving additional crop of the product.



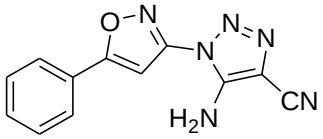
5-Amino-1-[5-(4-chlorophenyl)isoxazol-3-yl]-1*H*-1,2,3-triazole-4-carbonitrile 2a.

Yield 85%. Off-white powder. Decomp. > 250°C. ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 9.06 (bs, NH), 7.84 (AB, d, *J* = 8.6 Hz, 2H, Ar), 7.56 (AB, d, *J* = 8.6 Hz, 2H, Ar), 6.91 (s, 1H, isoxazole-C^{4}H), 3.36 (bs, NH); ^{13}C NMR (101 MHz, DMSO-d$_6$): δ 166.4 (1C, Isoxazole-C^5), 162.9 (1C, Isoxazole-C^3), 149.4 (1C, Triazole-C^5), 135.0 (1C, C-Cl), 129.6 (2C, Ar-C^{3,5}), 127.6 (2C, Ar-C^{2,6}), 126.7 (1C, Ar-C^4), 117.8 (1C, CN), 105.0 (1C, Ttriazole-C^4), 94.3 (1C, Isoxazole-C^4); IR (ν, cm^{-1}): 3419, 3305 (NH$_2$), 3143 (aromatic C-H stretchings), 2241 (C≡N), 1649, 1614, 1543, 1468 (cyclic C=C, C=N, CON), 1013, 951, 831, 802 (aromatic C-H deformations); HRMS (ESI-TOF) (*m*/*z*) [M+H]$^+$ calcd for C$_{12}$H$_8$ClN$_6$O 287.0448, found 287.0444.



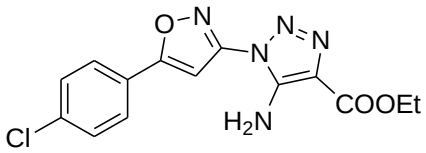
5-Amino-1-[5-(4-bromophenyl)isoxazol-3-yl]-1*H*-1,2,3-triazole-4-carbonitrile 2b.

Yield 88%. White powder. Decomp. > 250°C. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.03 – 7.92 (m, 2H, Ar), 7.84 – 7.74 (m, 3H, Ar + Isoxazole-C^{4}H), 3.30 (bs, NH); ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 170.0 (1C, Isoxazole-C^5), 157.6 (1C, Isoxazole-C^3), 147.5 (1C, Triazole-C^5), 132.5 (2C, Ar), 127.9 (2C, Ar), 125.1 (1C, Ar), 125.0 (1C, Ar), 112.7 (1C, CN), 101.3 (1C, Triazole-C^4), 95.4 (1C, Isoxazole-C^4); IR (ν, cm^{-1}): 3307 (NH$_2$), 2235 (C≡N), 1655, 1616, 1562, 1525, 1462 (cyclic C=C, C=N, CON), 825, 779 (aromatic C-H deformations); HRMS (ESI-TOF) (*m*/*z*) [M+H]$^+$ calcd for C$_{12}$H$_8$BrN$_6$O 330.9943, found 330.9937.



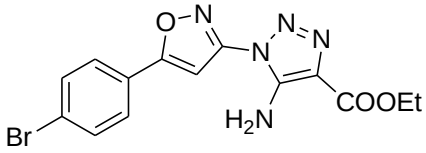
5-Amino-1-[5-phenylisoxazol-3-yl]-1*H*-1,2,3-triazole-4-carbonitrile 2c.

Yield 95%. White powder. Decomp. > 250°C. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 9.04 (bs, NH), 7.83 – 7.75 (m, 2H, Ar), 7.54 – 7.43 (m, 3H, Ar), 6.85 (s, 1H, Isoxazole-C^4), 3.62 (bs, NH); ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 167.6 (1C, Isoxazole-C^5), 162.8 (1C, Isoxazole-C^3), 149.3 (1C, Triazole-C^5), 130.4 (1C, ArC^4), 129.5 (2C, Ar), 127.9 (1C, Ar), 125.7 (2C, Ar), 117.9 (1C, CN), 105.0 (1C, Triazole-C^4); 93.7 (1C, Isoxazole-C^4); IR (ν, cm^{-1}): 3311 (NH$_2$), 2233 (CN), 1636, 1614, 1598, 1577, 1531, 1462, 1418 (C=C, C=N, CON), 789, 751 (aromatic C-H deformations); HRMS (ESI-TOF) (*m*/*z*) [M+H]$^+$ calcd for C$_{12}$H$_9$N$_6$O 253.0838, found 253.0836.



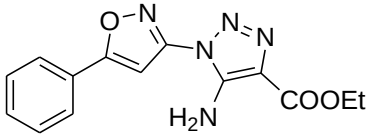
Ethyl 5-amino-1-[5-(4-chlorophenyl)isoxazol-3-yl]-1*H*-1,2,3-triazole-4-carboxylate 3a.

Yield 89%. White powder. Decomp. > 250°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.66 (bs, NH), 7.90 – 7.81 (m, 2H, Ar-C^{3,5}H), 7.61 – 7.53 (m, 2H, Ar C^{2,6}H), 7.12 (s, 1H, Isoxazole-C^{4}H), 4.29 (q, *J* = 7.1 Hz, 2H, CH_2), 1.30 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.8 (1C, Isoxazole-C^{5}), 162.0 (1C, COOEt), 160.9 (Isoxazole-C^{3}), 147.1 (1C, Triazole-C^{5}), 135.5 (1C, ArC^{4}-Cl), 129.7 (2C, ArC^{2,6}), 127.7 (2C, ArC^{3,5}), 126.4 (1C, ArC^{1}), 123.2 (1C, Triazole-C^{4}), 94.6 (1C, Isoxazole-C^{4}), 60.7 (1C, CH_2), 14.6 (1C, CH_3); IR (ν, cm^{-1}): 3441, 3300 (NH_2), 1708 (CO-ester), 1622, 1539, 1471 (C=C, C=N, CON), 834, 804, 780 (aromatic C-H deformations); HRMS (ESI-TOF) (*m*/*z*) [M+H]$^{+}$ calcd for $C_{14}H_{13}ClN_5O_3$ 334.0707, found 334.0704.



Ethyl 5-amino-1-[5-(4-bromophenyl)isoxazol-3-yl]-1*H*-1,2,3-triazole-4-carboxylate 3b.

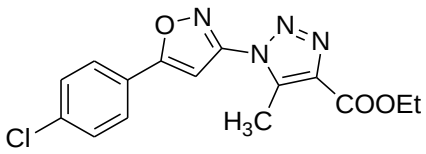
Yield 72%. White powder. Decomp. > 250°C. ^{1}H NMR (400 MHz, DMSO-d_6, T = 75ºC) δ 7.78 – 7.65 (m, 4H, Ar), 7.09 (s, 1H, Isoxazole-C^{4}H), 4.34 (q, *J* = 7.1 Hz, 2H, CH_2), 1.31 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6, T = 75ºC) δ 168.0 (1C, Isoxazole-C^{5}), 161.9 (1C, COOEt), 160.9 (1C, Isoxazole-C^{3}), 147.0 (1C, Triazole-C^{5}), 132.6 (2C, Ar), 127.9 (2C, Ar), 126.8 (1C, Ar), 124.2 (1C, Ar), 123.4 (1C, Triazole-C^{4}), 94.6 (1C, Isoxazole-C^{4}), 60.8 (1C, CH_2), 14.5 (1C, CH_3); IR (ν, cm^{-1}): 3438, 3263 (NH_2), 3132 (aromatic C-H stretchings), 1711 (C=O), 1679, 1620, 1538 (cyclic C=C, C=N, CON), 832, 809, 776 (aromatic C-H deformations); HRMS (ESI-TOF) (*m*/*z*) [M+H]$^{+}$ calcd for $C_{14}H_{13}BrN_5O_3$ 378.0202, found 378.0198.



Ethyl 5-amino-1-(5-phenylisoxazol-3-yl)-1*H*-1,2,3-triazole-4-carboxylate 3c.

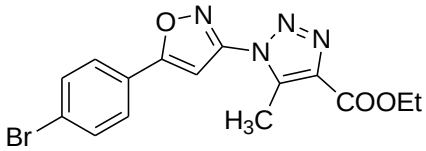
Yield 60%. White powder. Decomp. > 250°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.79 (bs, NH), 7.85 – 7.76 (m, 2H), 7.56 – 7.45 (m, 3H), 7.07 (s, 1H, Isoxazole-C^{4}), 4.33 (q, *J* = 7.1 Hz, 2H, CH_2), 1.30 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.0 (1C, Isoxazole-C^{5}), 161.9 (1C, COOEt), 160.7 (1C, Isoxazole-C^{3}), 146.7 (1C, Triazole-C^{5}), 130.8 (1C, ArC^{4}), 129.6 (2C, Ar), 127.5 (1C, ArC^{1}), 125.9 (2C, Ar), 123.1 (1C, Triazole-C^{4}), 94.0 (1C, Isoxazole-C^{4}), 60.8 (1C, CH_2), 14.6 (1C, CH_3); IR (ν, cm^{-1}): 3263 (NH_2), 3130 (aromatic C-H stretchings), 1680 ($\nu_{C=O}$), 1616,

1598, 1577, 1530, 1509 (cyclic C=C, C=N, CON), 1227 (C-O-C in ester), 1027, 763 (aromatic C-H deformations); HRMS (ESI-TOF) (*m*/*z*) $[M+H]^+$ calcd for $C_{14}H_{14}N_5O_3$ 300.1097, found 300.1091.



Ethyl 1-[5-(4-chlorophenyl)isoxazol-3-yl]-5-methyl-1*H*-1,2,3-triazole-4-carboxylate 4a.

Yield 92%. White powder. Decomp. > 250°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.02 – 7.97 (m, 2H, Ar), 7.72 (s, 1H, Isoxazole-C^4), 7.65 – 7.60(m, 2H, Ar), 4.37 (q, *J* = 7.1 Hz, 2H, CH_2), 2.79 (s, 3H, Triazole-CH_3), 1.34 (t, *J* = 7.1 Hz, 3H, CH_2-$\underline{CH_3}$); ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.9 (1C, Isoxazole-C^5), 161.0 (1C, $\underline{C}$(O)OEt), 158.6 (1C, Isoxazole-C^3), 140.5 (1C, Triazole-C^4), 137.3 (1C, Triazole-C^5), 136.7 (1C, ArC^{4}Cl), 130.0 (2C, Ar), 129.9 (2C, Ar, minor form), 128.2 (2C, Ar), 128.1 (2C, Ar, minor form), 125.2 (1C, ArC^1), 97.1 (1C, Isoxazole-C^4), 96.8 (1C, Isoxazole-C^4, minor form), 61.2 (1C, $\underline{C}H_2$-CH_3), 14.5 (1C, CH_2-$\underline{C}H_3$), 10.5 (1C, Isoxazole-$\underline{C}H_3$), 10.4 (1C, Isoxazole-$\underline{C}H_3$, minor form); IR (ν, cm^{-1}): 3132, 3093 (aromatic C-H stretchings), 1727 ($\nu_{C=O}$), 1651, 1612, 1526, 1469 (cyclic C=C, C=N, CON), 1198, 1079 (C-O-C in ester), 849, 813 (aromatic C-H deformations); HRMS (ESI-TOF) (*m*/*z*) $[M+H]^+$ calcd for $C_{15}H_{14}ClN_4O_3$ 333.0754, found 333.0739.



Ethyl 1-[5-(4-bromophenyl)isoxazol-3-yl]-5-methyl-1*H*-1,2,3-triazole-4-carboxylate 4b.

Yield 93%. White powder. Decomp. > 250°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.97 (d, *J* = 8.5 Hz, 2H, Ar), 7.82 (s, 1H, Isoxazole-C^{4}H), 7.81 (d, *J* = 8.7 Hz, 2H, Ar), 4.36 (q, *J* = 7.1 Hz, 2H, CH_2), 2.80 (s, 3H, Triazole-CH_3), 1.33 (t, *J* = 7.1 Hz, 3H, CH_2-$C\underline{H_3}$); ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.9 (1C, Isoxazole-C^5), 161.0 (1C, $\underline{C}$(O)OEt), 158.6 (1C, Isoxazole-C^3), 140.6 (1C, Triazole-C^4), 137.2 (1C, Triazole-C^5), 132.9 (2C, Ar), 128.3 (2C, Ar), 125.49 (1C, Ar), 125.48 (1C, Ar), 97.1 (1C, Isoxazole-C^4), 61.3 (1C, $\underline{C}H_2$-CH_3), 14.5 (1C, CH_2-$\underline{C}H_3$), 10.6 (1C, Isoxazole-$\underline{C}H_3$); IR (ν, cm^{-1}): 3132, 3089 (aromatic C-H stretchings), 1732 ($\nu_{C=O}$), 1608, 1525, 1468 (cyclic C=C, C=N, CON), 1196, 1080 (C-O-C in ester), 847, 814 (aromatic C-H deformations); HRMS (ESI-TOF) (*m*/*z*) $[M+H]^+$ calcd for $C_{15}H_{14}BrN_4O_3$ 377.0249, found 377.0244.

References

[S1] K. Banert, in *Organic Azides – Syntheses and Applications*, eds. S. Bräse and K. Banert, John Wiley & Sons, Chichester, UK, 2010, pp. 115-166.

[S2] P. S. Lemport, I. V. Smolyar, V. N. Khrustalev, V. A. Roznyatovsky, A. V. Popov, V. A. Kobelevskaya, I. B. Rozentsveig and V. G. Nenajdenko, *Org. Chem. Front.*, 2019, **6**, 335.

NMR and IR spectra of synthesized compounds

5-Amino-1-[5-(4-chloro-phenyl)-isoxazol-3-yl]-1*H*-[1,2,3]triazole-4-carbonitrile 2a

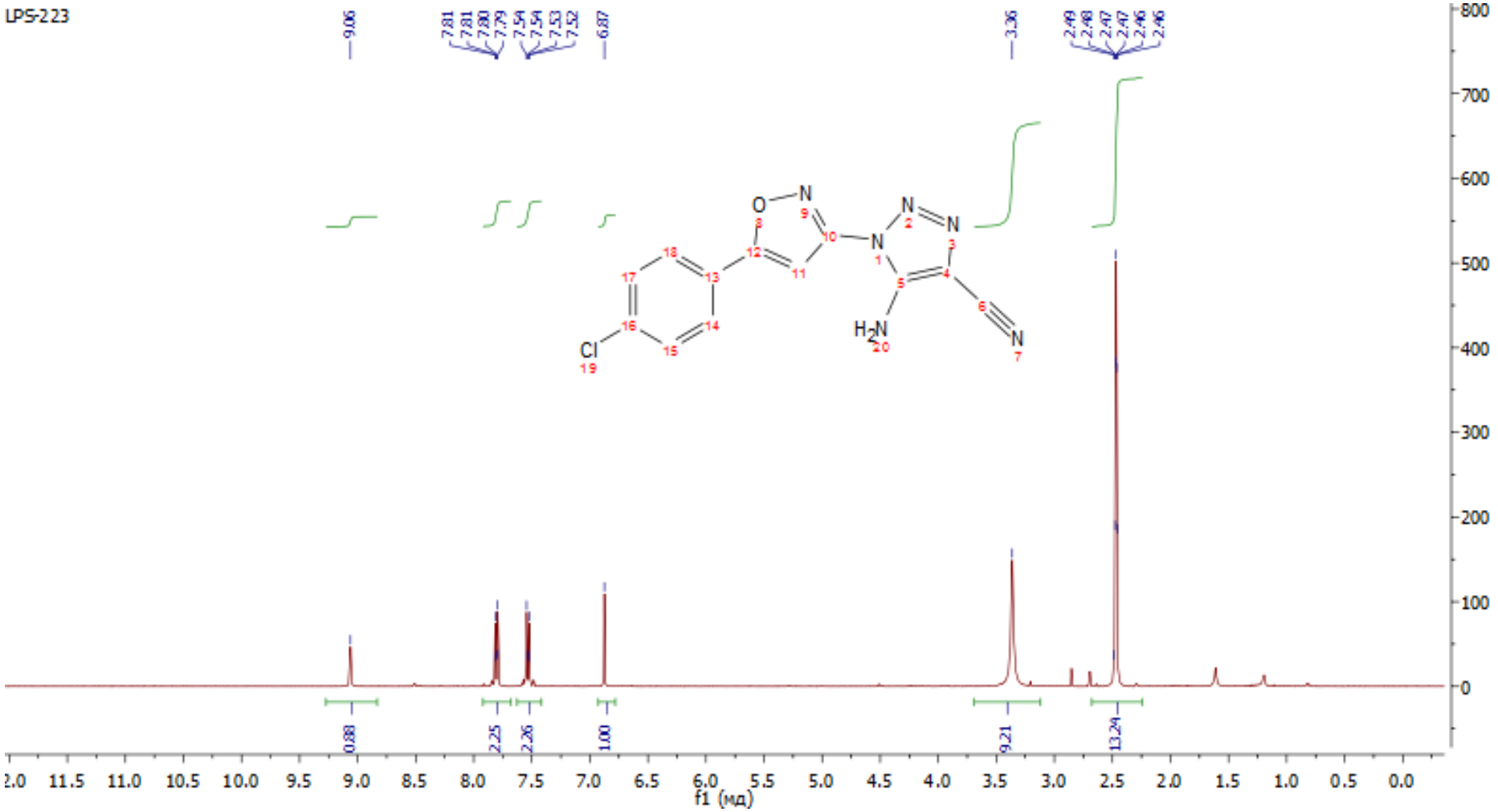


Figure S1. ^{1}H NMR spectrum (DMSO-d$_6$) of **2a**

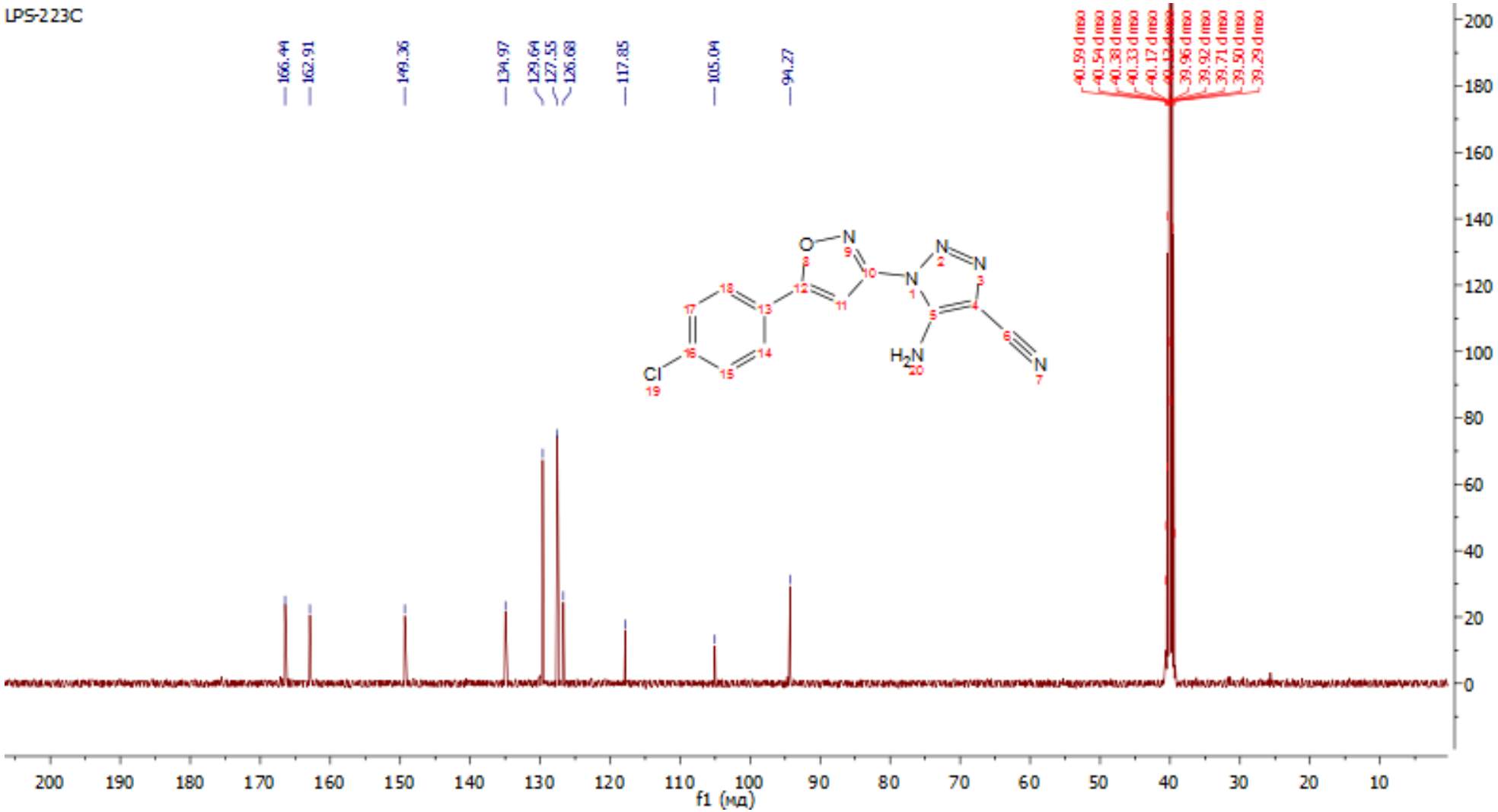


Figure S2. ^{13}C NMR spectrum (DMSO-d_6) of **2a**

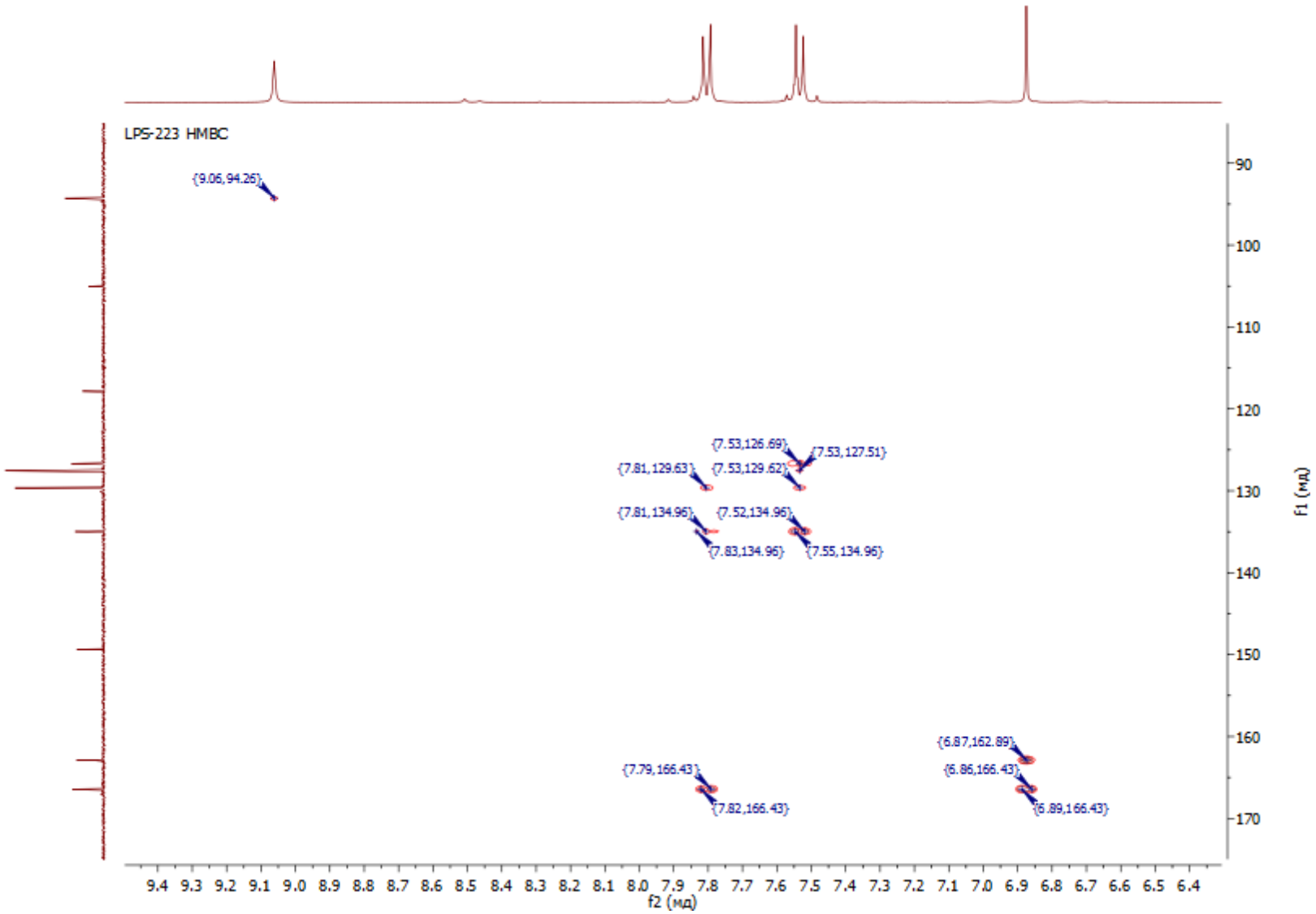


Figure S3. $^{1}H/^{13}C$ HMBC NMR (DMSO-d_6) of **2a**

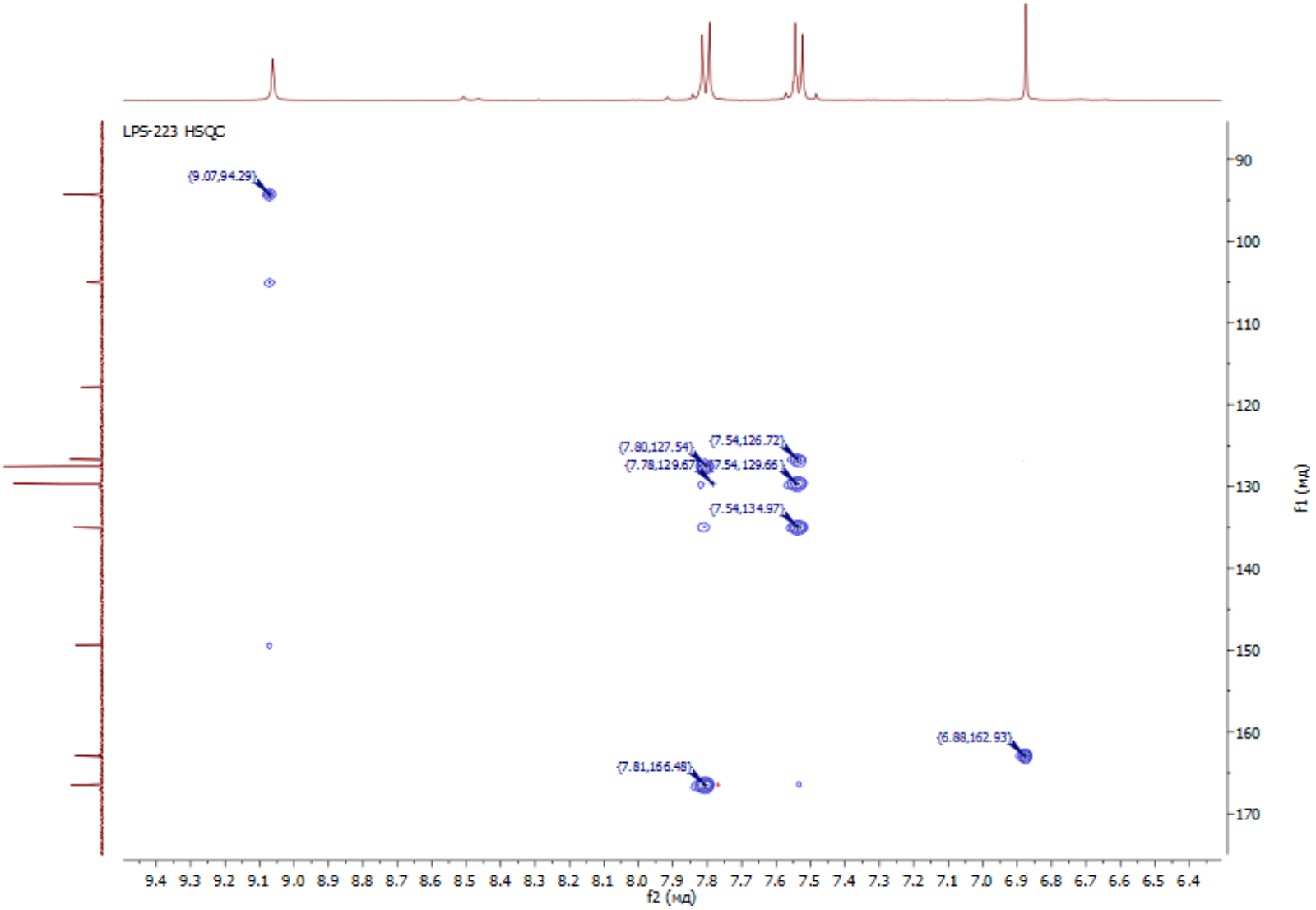


Figure S4. $^{1}H/^{13}C$ HSQC NMR (DMSO-d_6) of **2a**

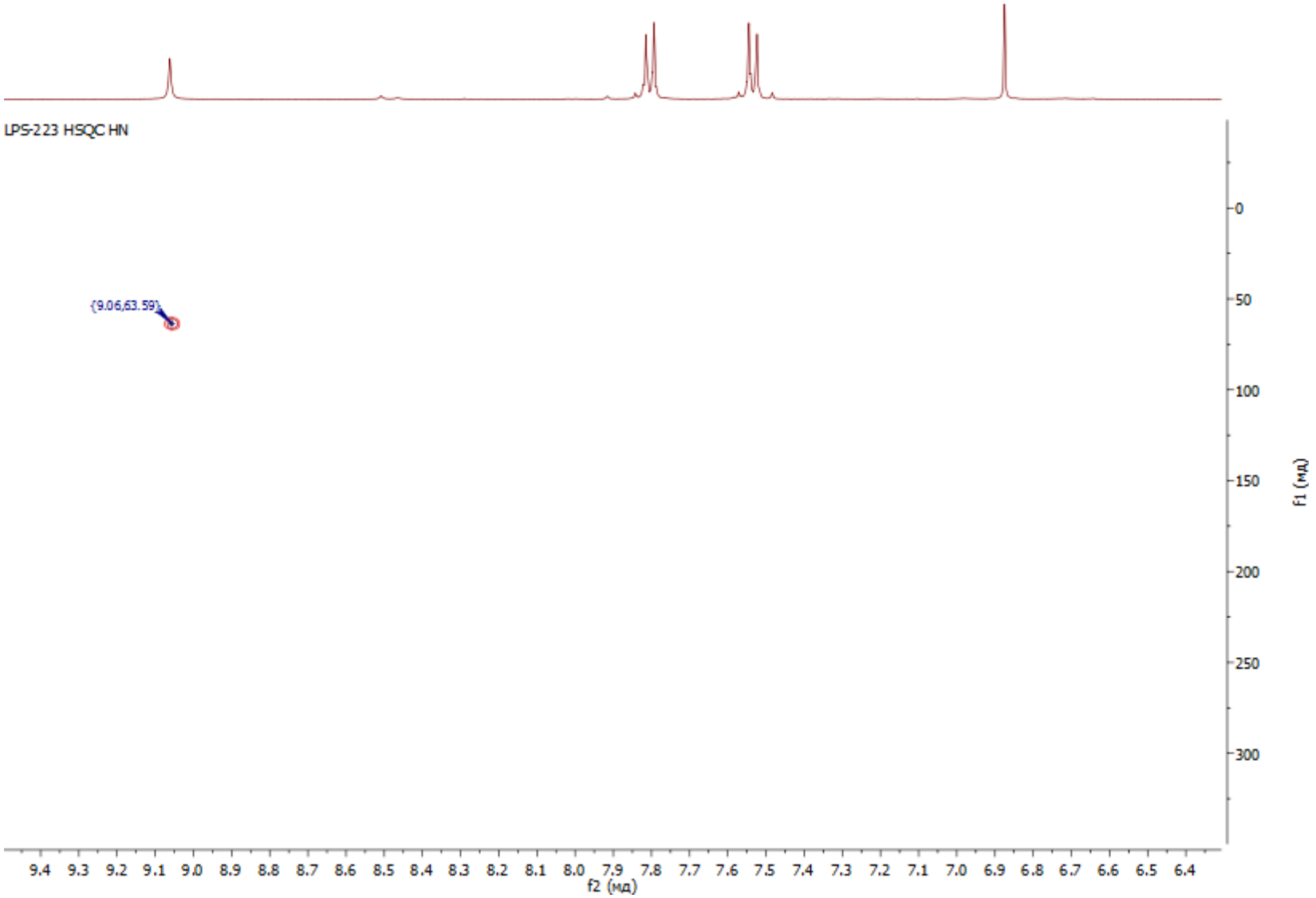


Figure S5. $^{1}H/^{15}N$ HSQC NMR (DMSO-d_6) of **2a**

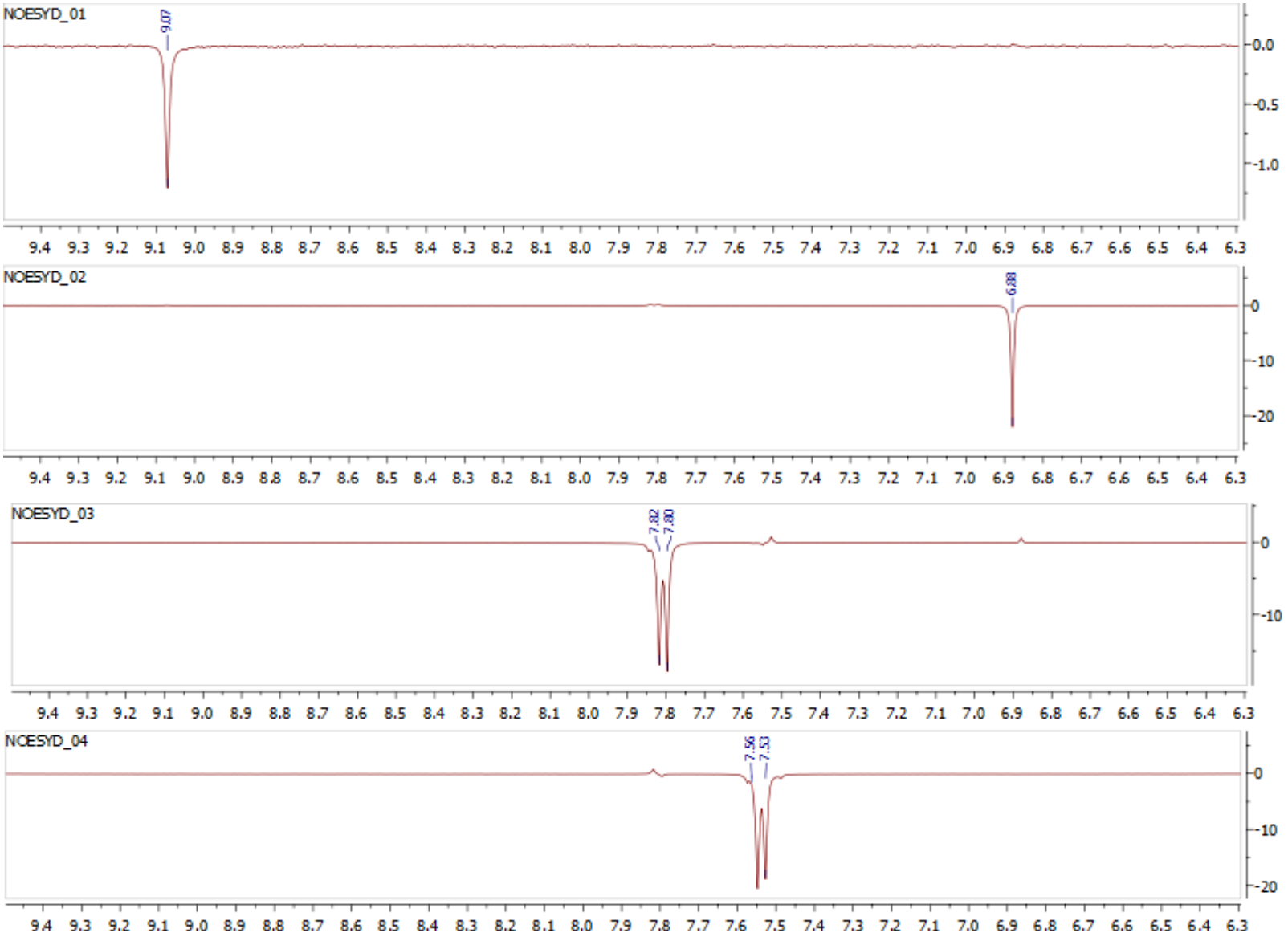


Figure S6. $^{1}H/^{1}H$ NOESY $^{1}H/^{1}H$ (DMSO-d_6) of **2a**

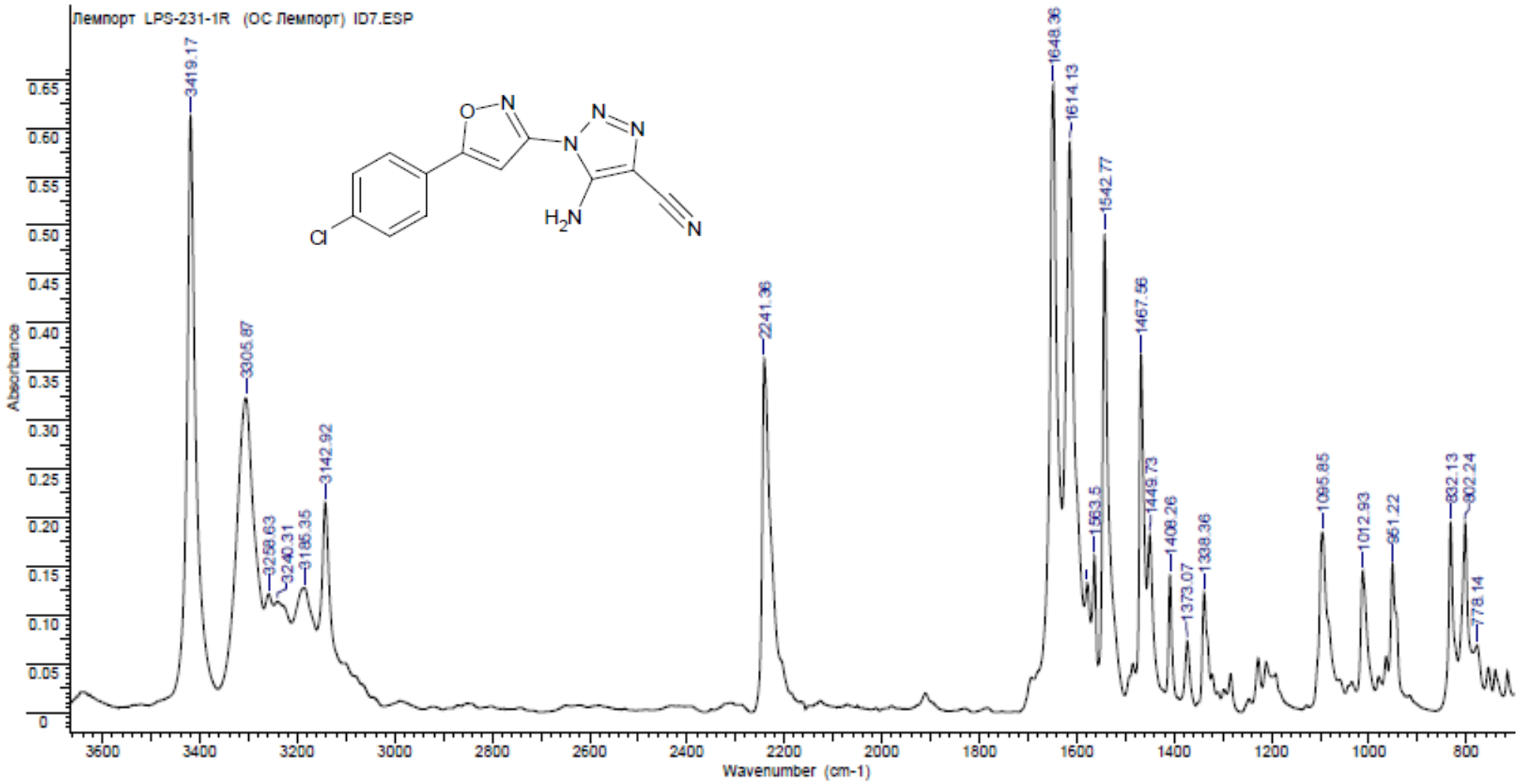


Figure S7. IR-spectrum of **2a**

5-Amino-1-[5-(4-bromo-phenyl)-isoxazol-3-yl]-1*H*-[1,2,3]triazole-4-carbonitrile 2b

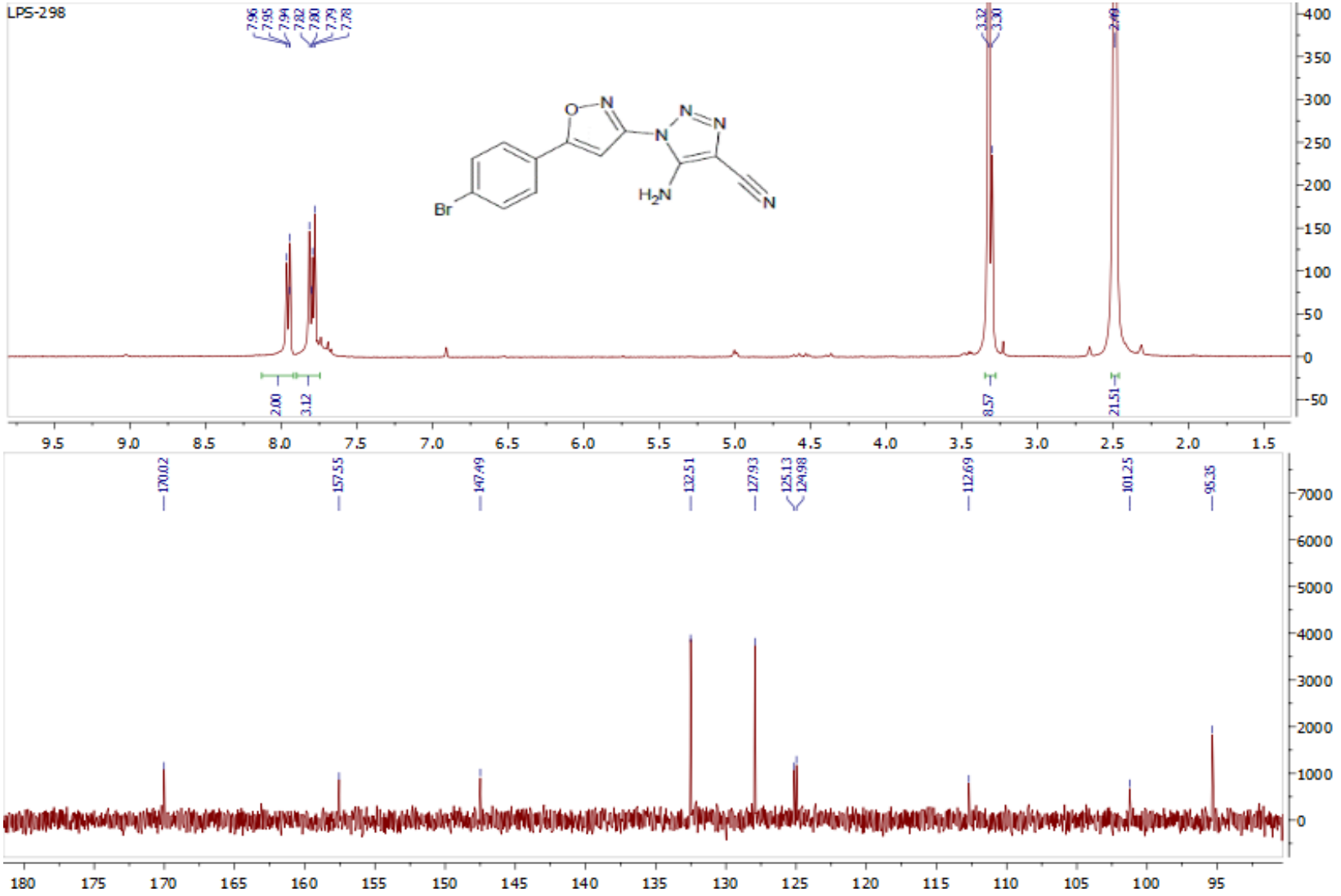


Figure 8. ^{1}H NMR (above) and ^{13}C NMR (below) spectra of **2b**

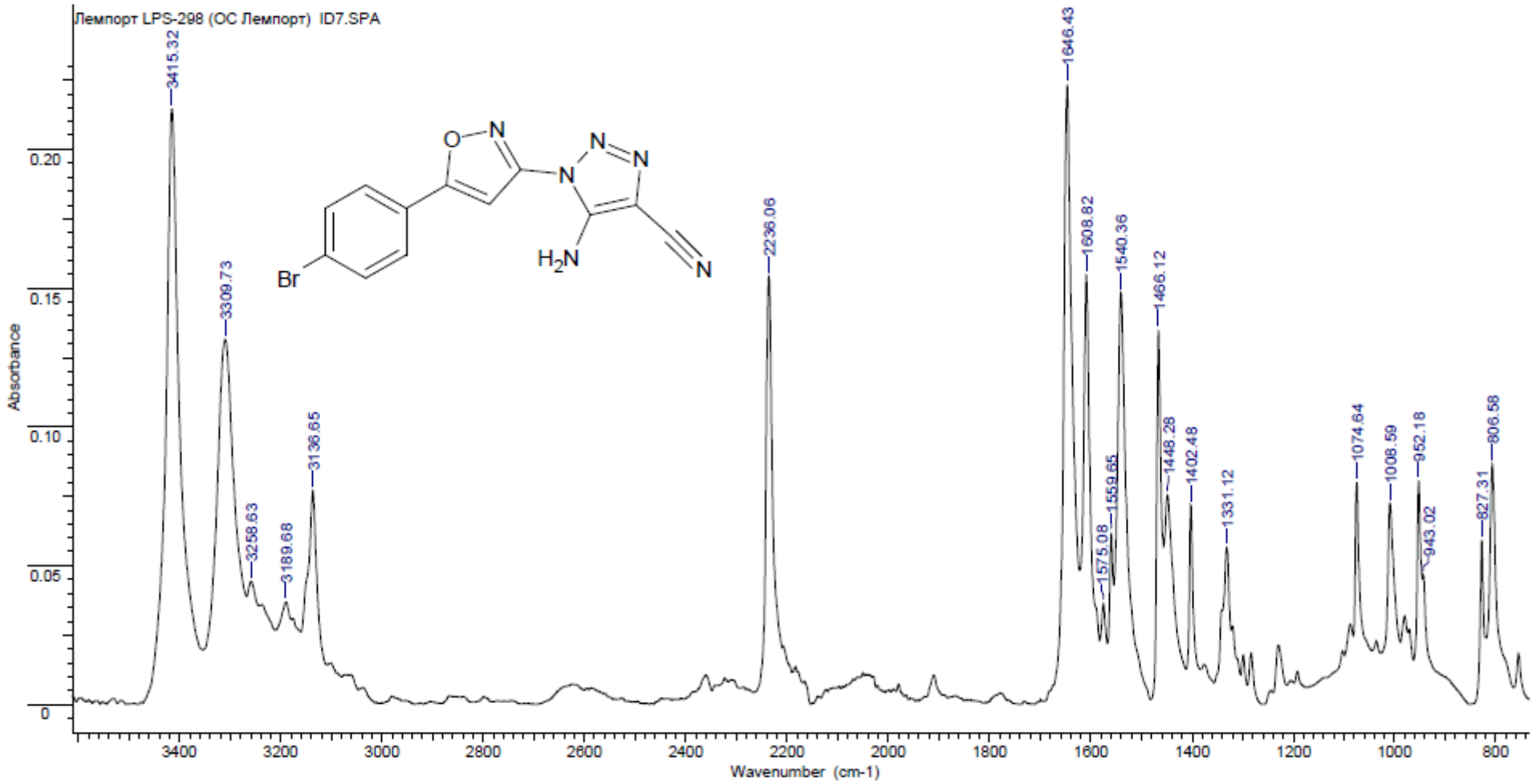


Figure S9. IR-spectrum of **2b**

5-Amino-1-(5-phenyl-isoxazol-3-yl)-1*H*-[1,2,3]triazole-4-carbonitrile 2c

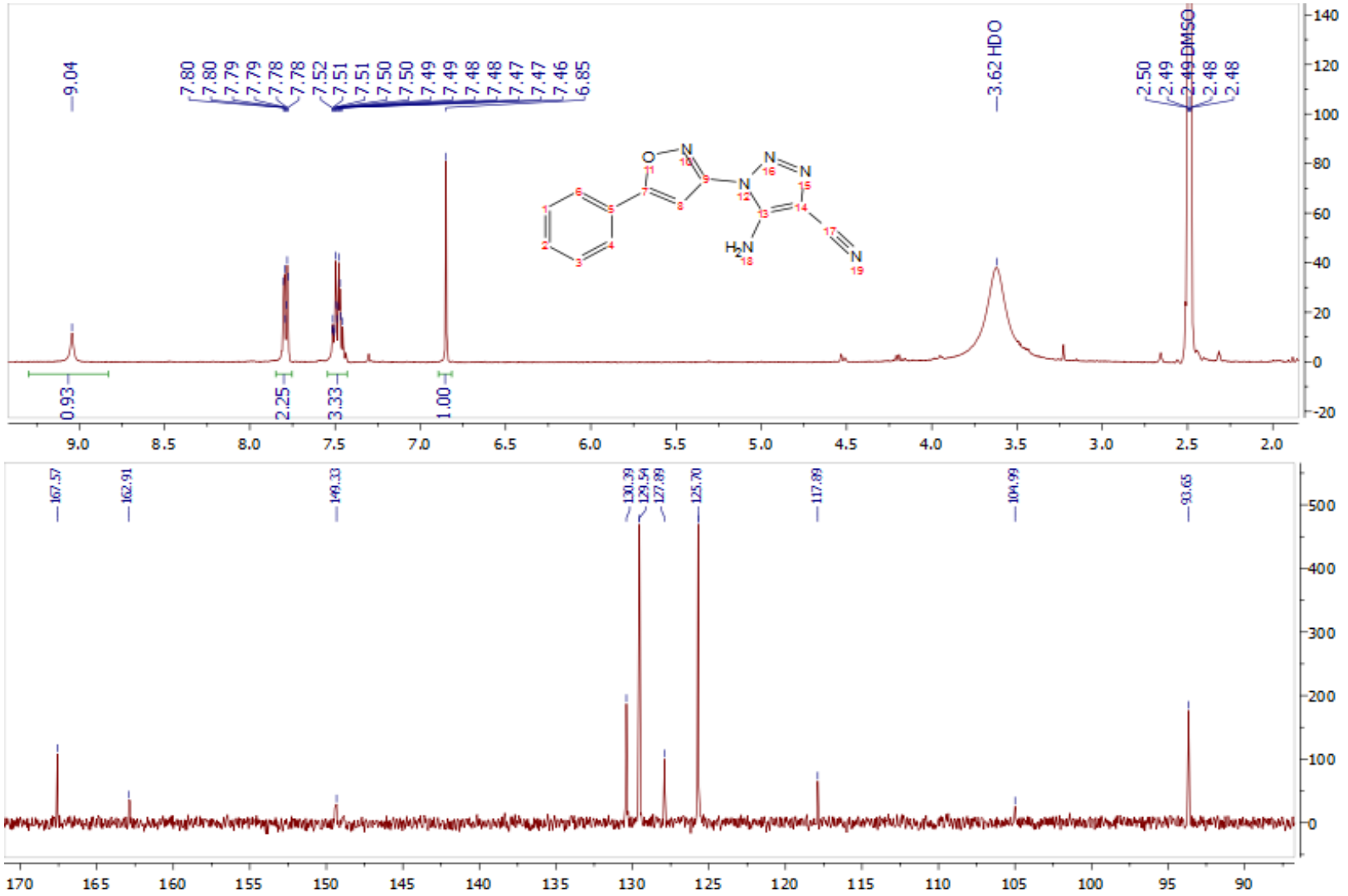


Figure S10. ^{1}H NMR (above) and ^{13}C NMR (below) spectra of **2c**

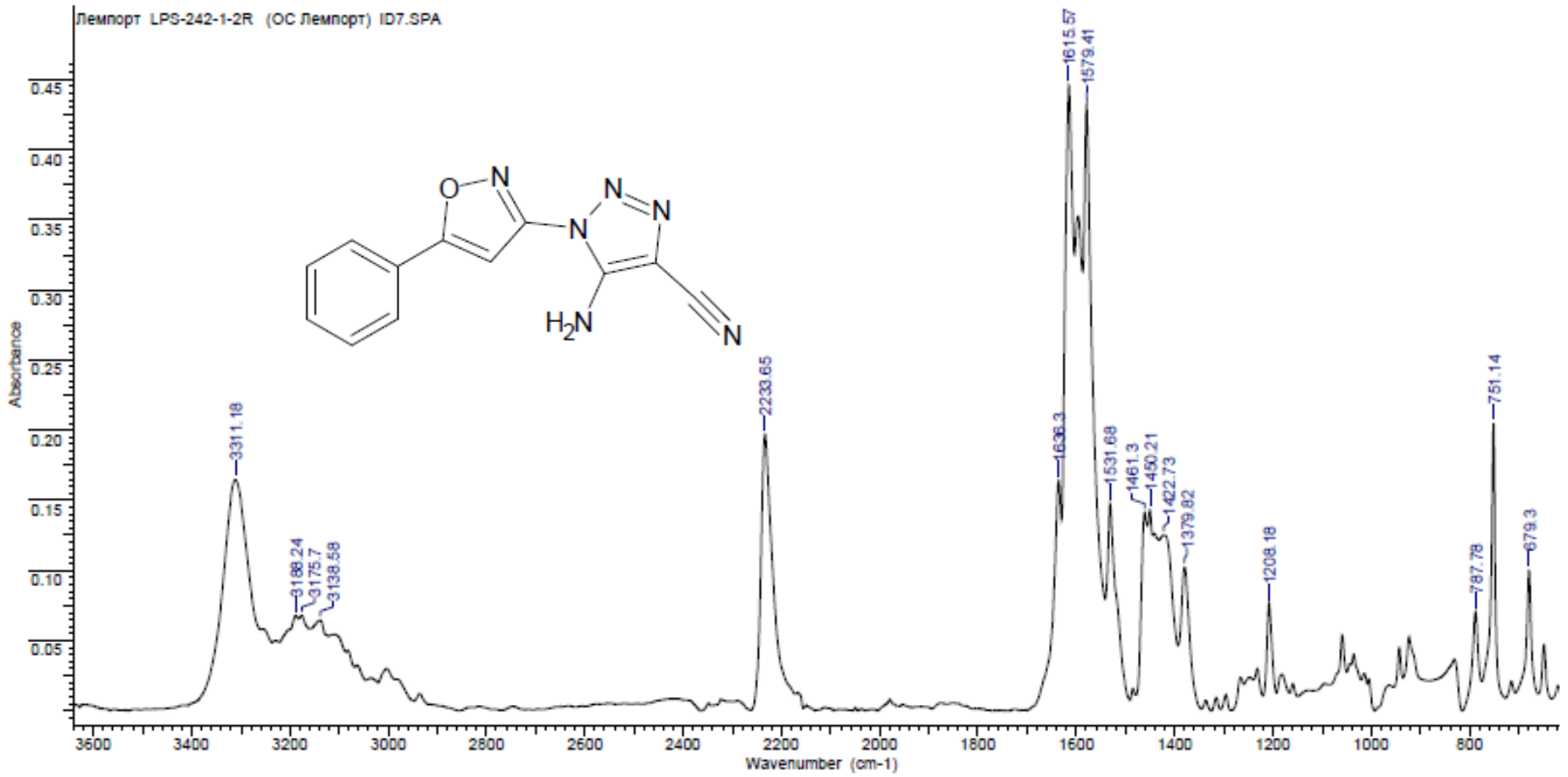


Figure S11. IR-spectrum of **2c**

5-Amino-1-[5-(4-chloro-phenyl)-isoxazol-3-yl]-1*H*-[1,2,3]triazole-4-carboxylic acid ethyl ester 3a

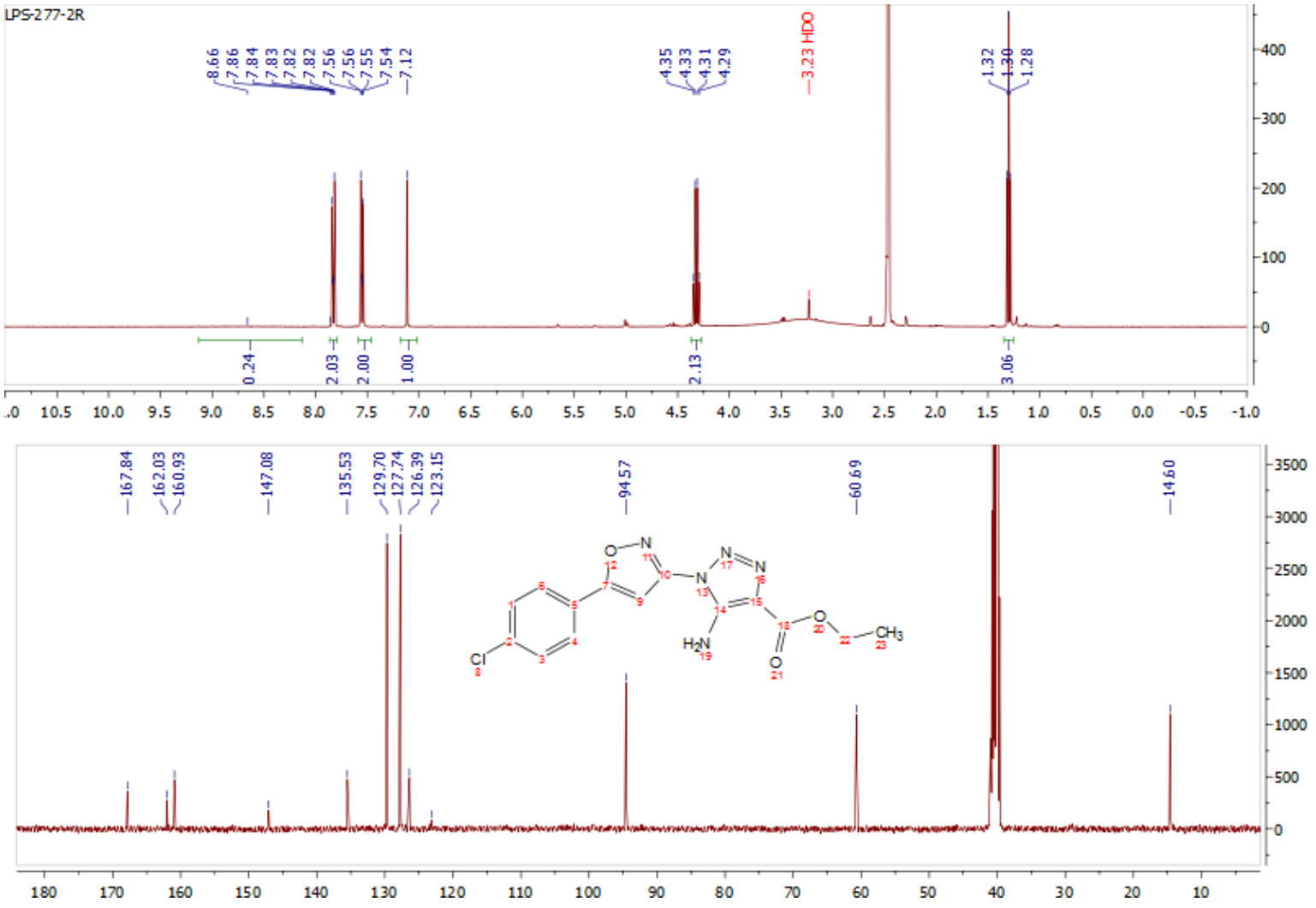


Figure S12. ^{1}H NMR (above) and ^{13}C NMR (below) spectra of **3a** recorded at 60^{o}C

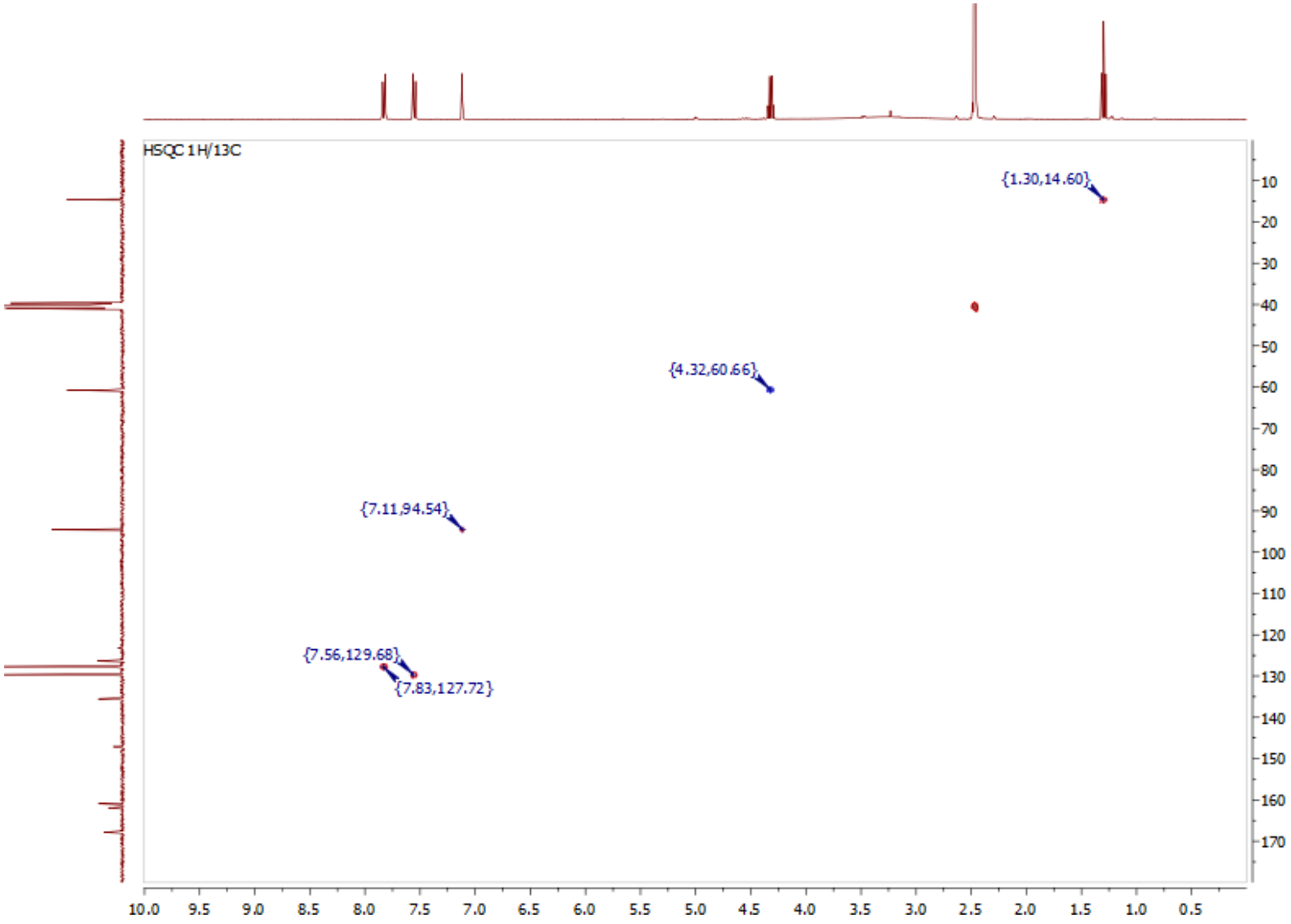


Figure S13. $^{1}H/^{13}C$ HSQC NMR of **3a**

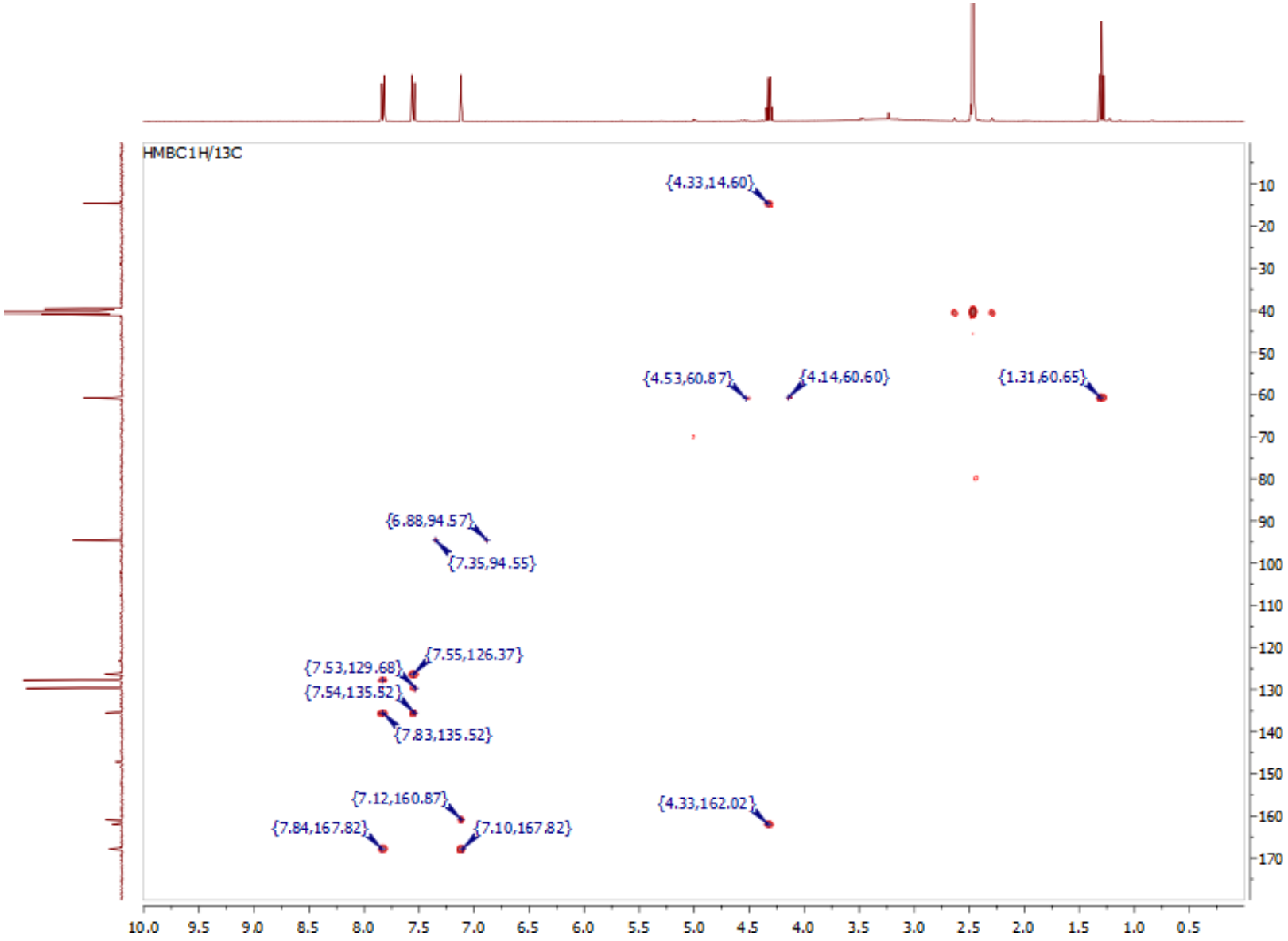


Figure S14. $^{1}H/^{13}C$ HMBC NMR of **3a**

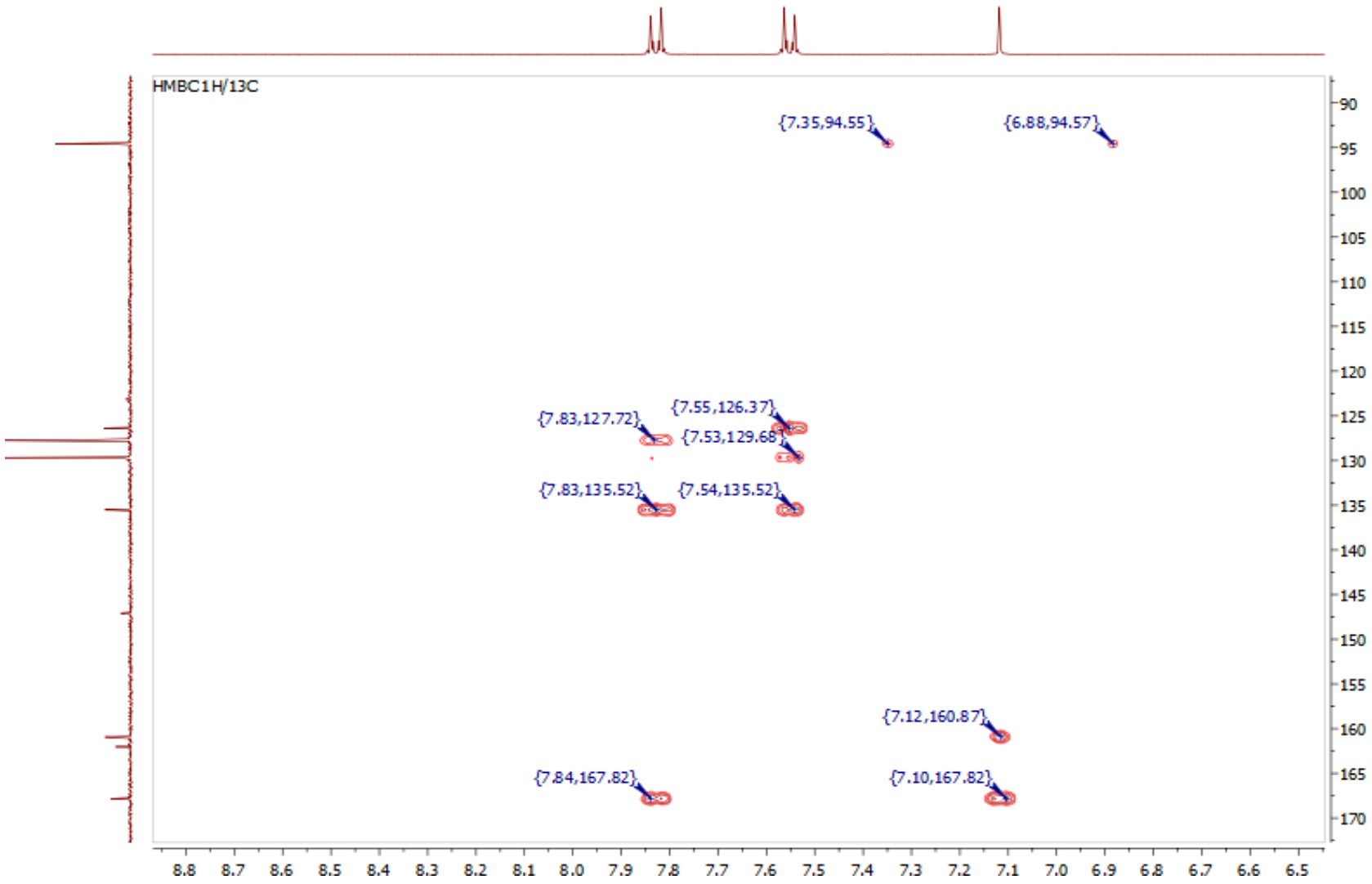


Figure S15. $^{1}H/^{13}C$ HMBC NMR (fragment) of **3a**

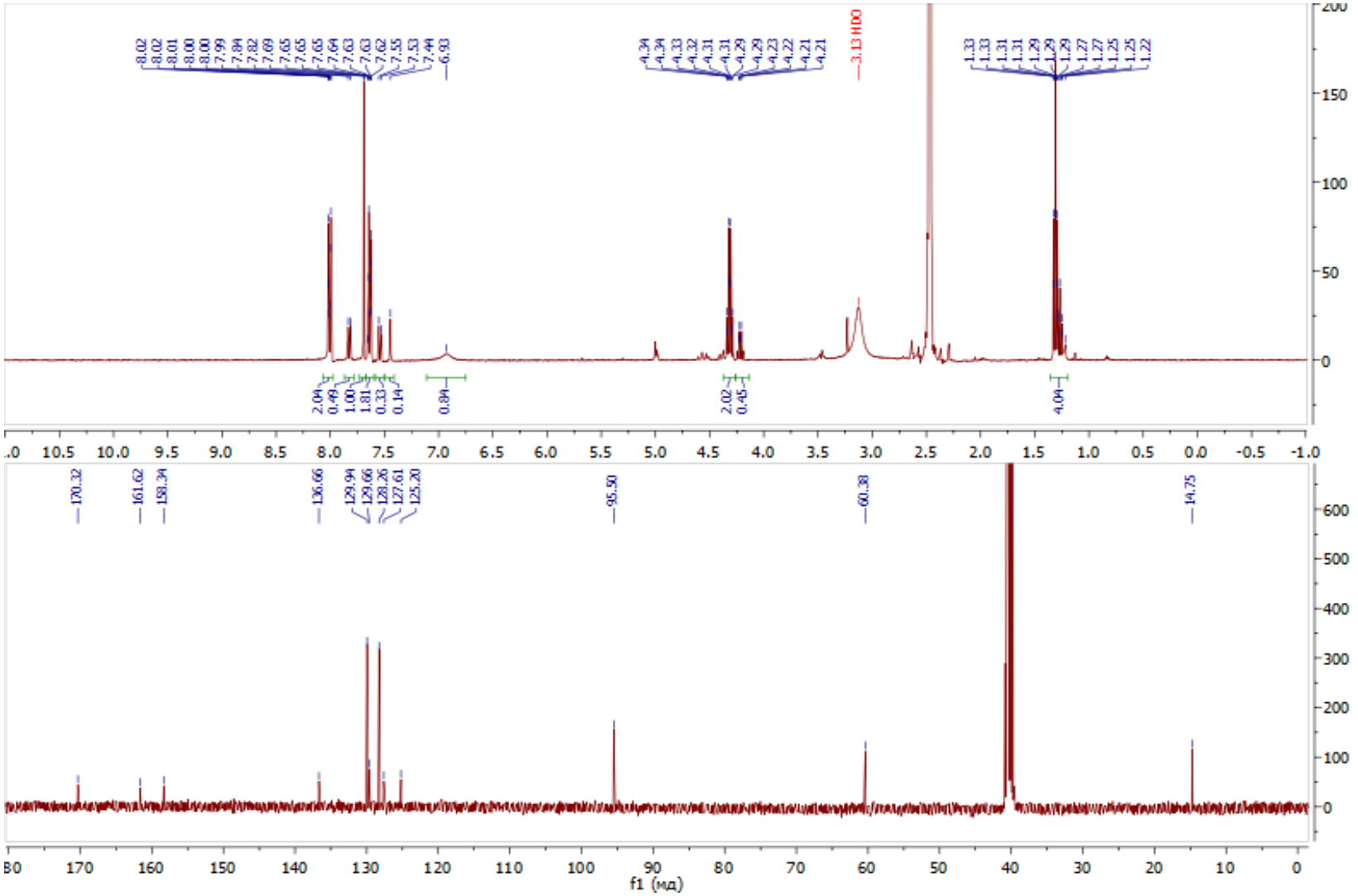


Figure S16. ^{1}H and ^{13}C NMR spectra of compound **3a** recorded at r.t. before warming in DMSO-d_6 at 60^{o}C (tautomeric form A)

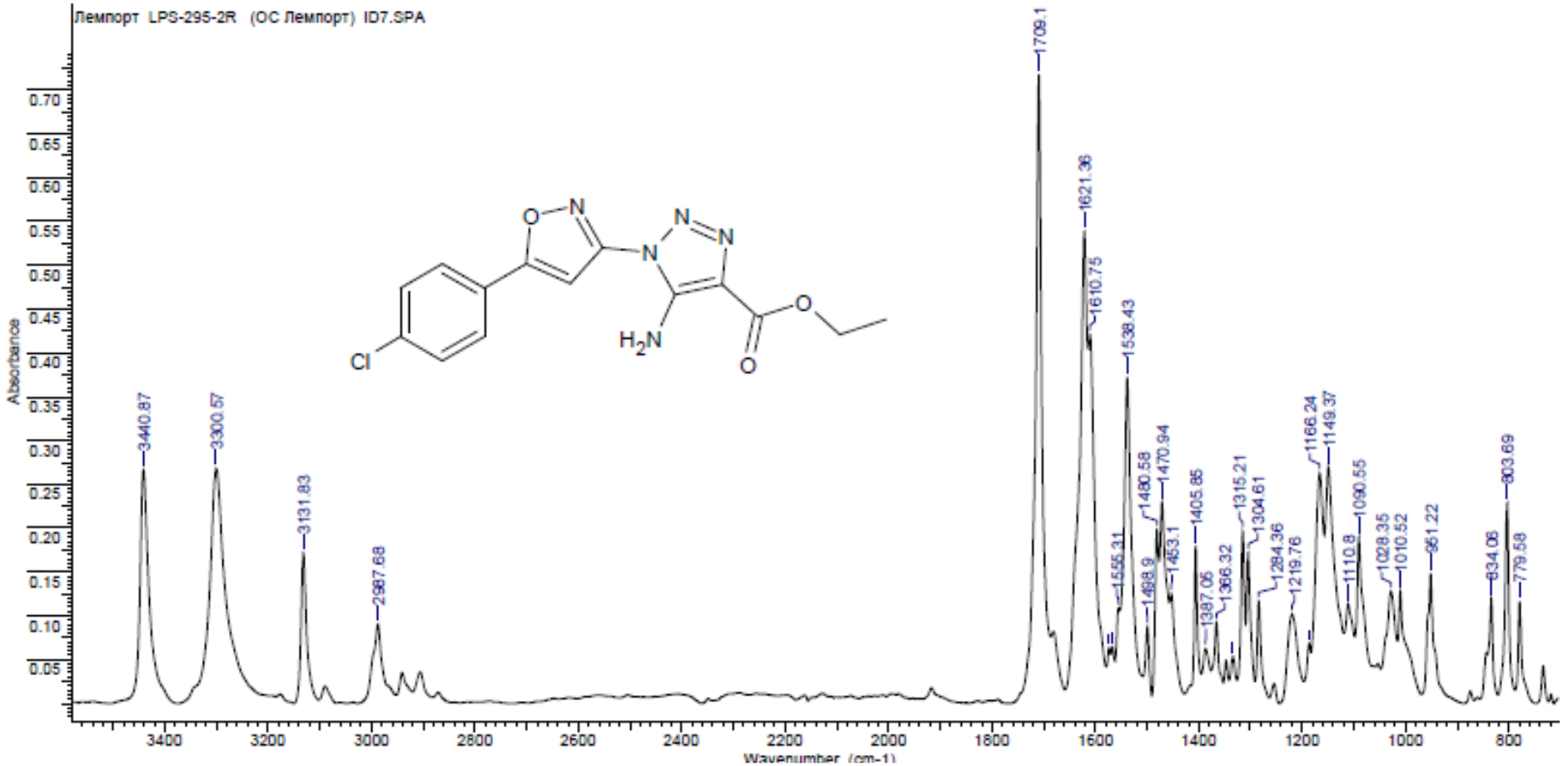


Figure S17. IR-spectrum of **3a**

5-Amino-1-[5-(4-chloro-phenyl)-isoxazol-3-yl]-1*H*-[1,2,3]triazole-4-carboxylic acid ethyl ester 3b

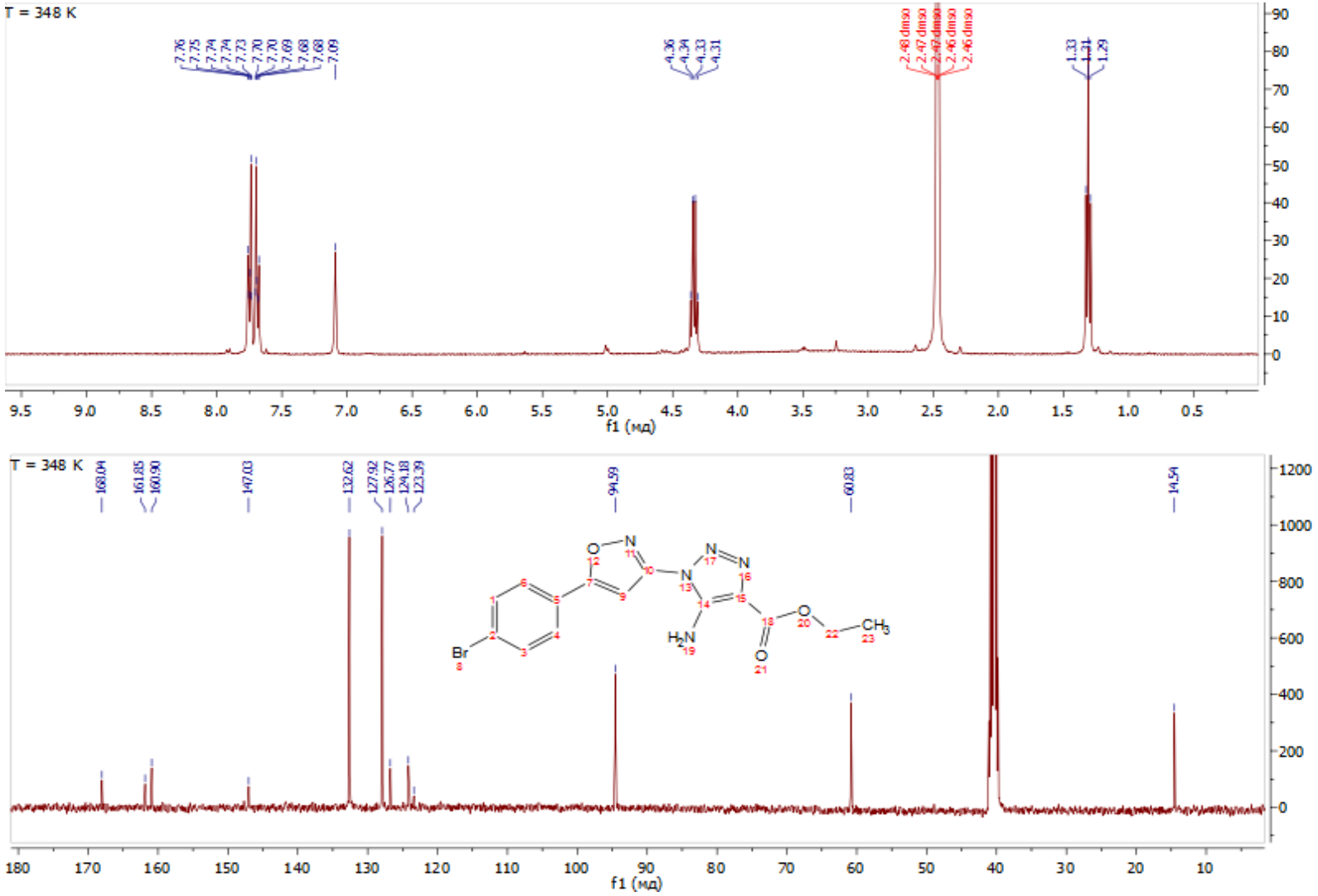


Figure S18. ^{1}H and ^{13}C NMR spectra of **3b** recorded at 75^{o}C

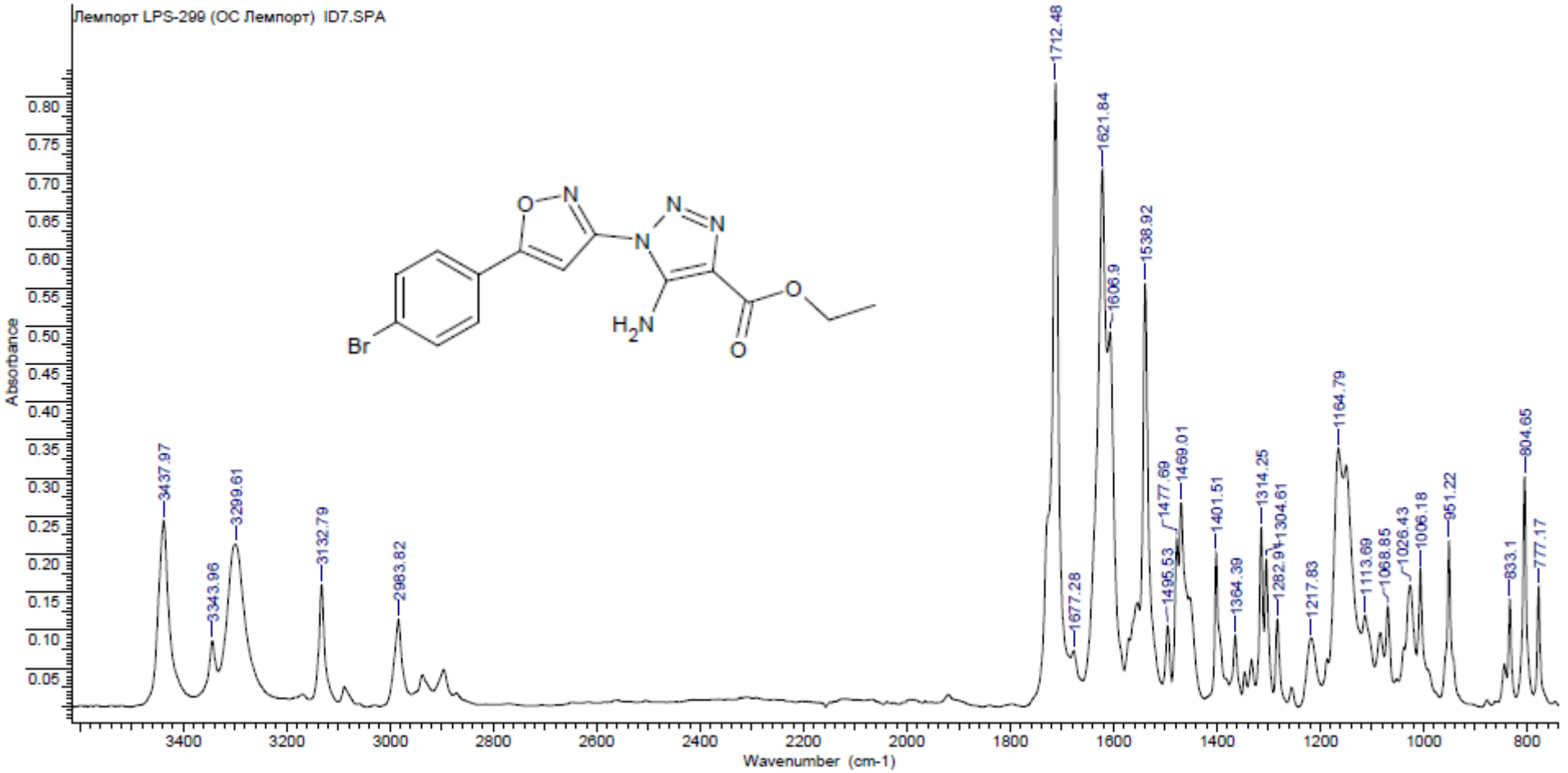


Figure S19. IR-spectrum of **3b**

5-Amino-1-(5-phenyl-isoxazol-3-yl)-1*H*-[1,2,3]triazole-4-carboxylic acid ethyl ester 3c

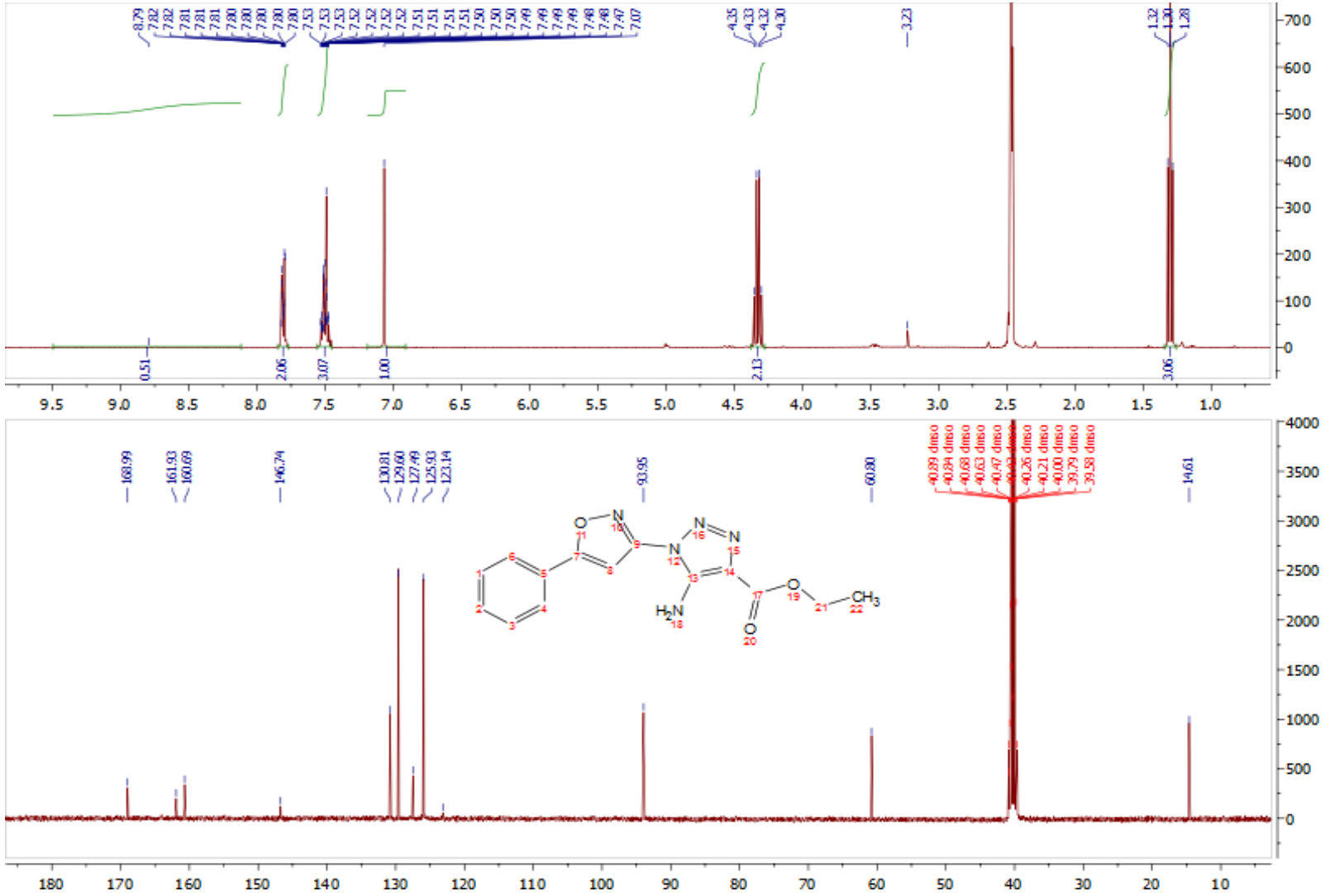


Figure S20. ^{1}H and ^{13}C NMR spectra of **3c** recorded at 60^{o}C

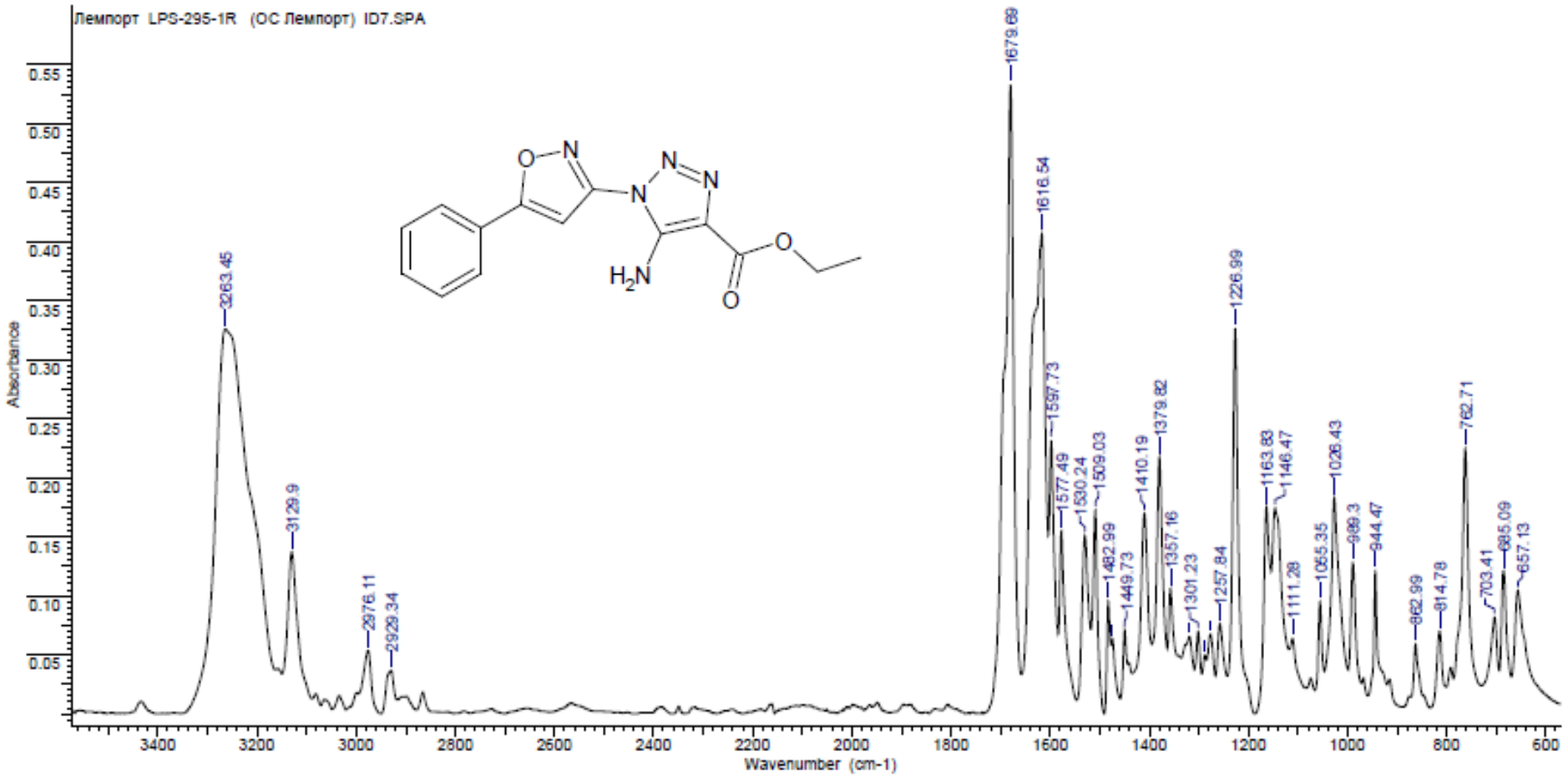


Figure S21. IR-spectrum of **3c**

1-[5-(4-Chloro-phenyl)-isoxazol-3-yl]-5-methyl-1*H*-[1,2,3]triazole-4-carboxylic acid ethyl ester **4a** (^{1}H, ^{13}C NMR, recorded at 60^{o}C)

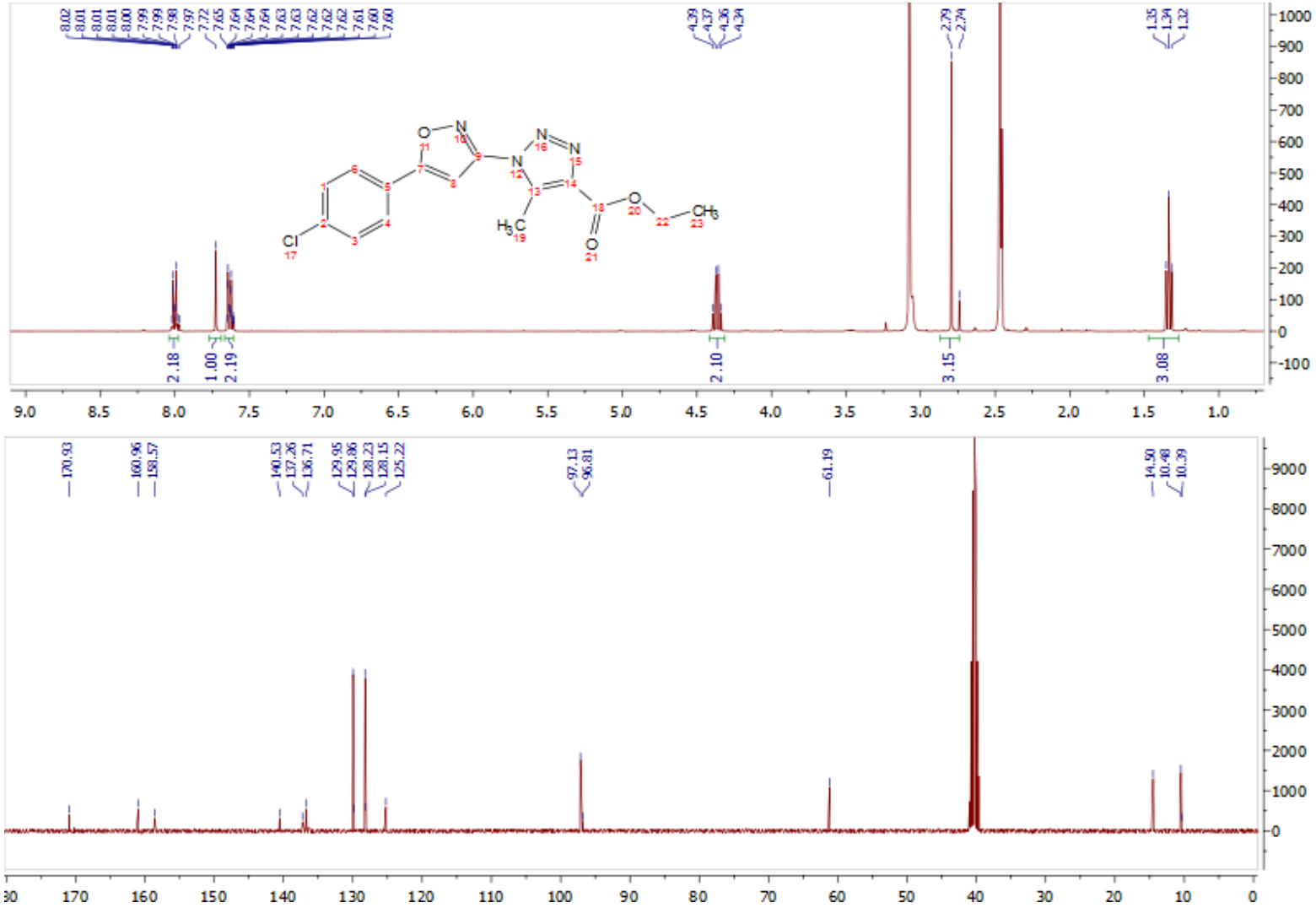


Figure S22. ^{1}H and ^{13}C NMR spectra of **4a** recorded at 60^{o}C

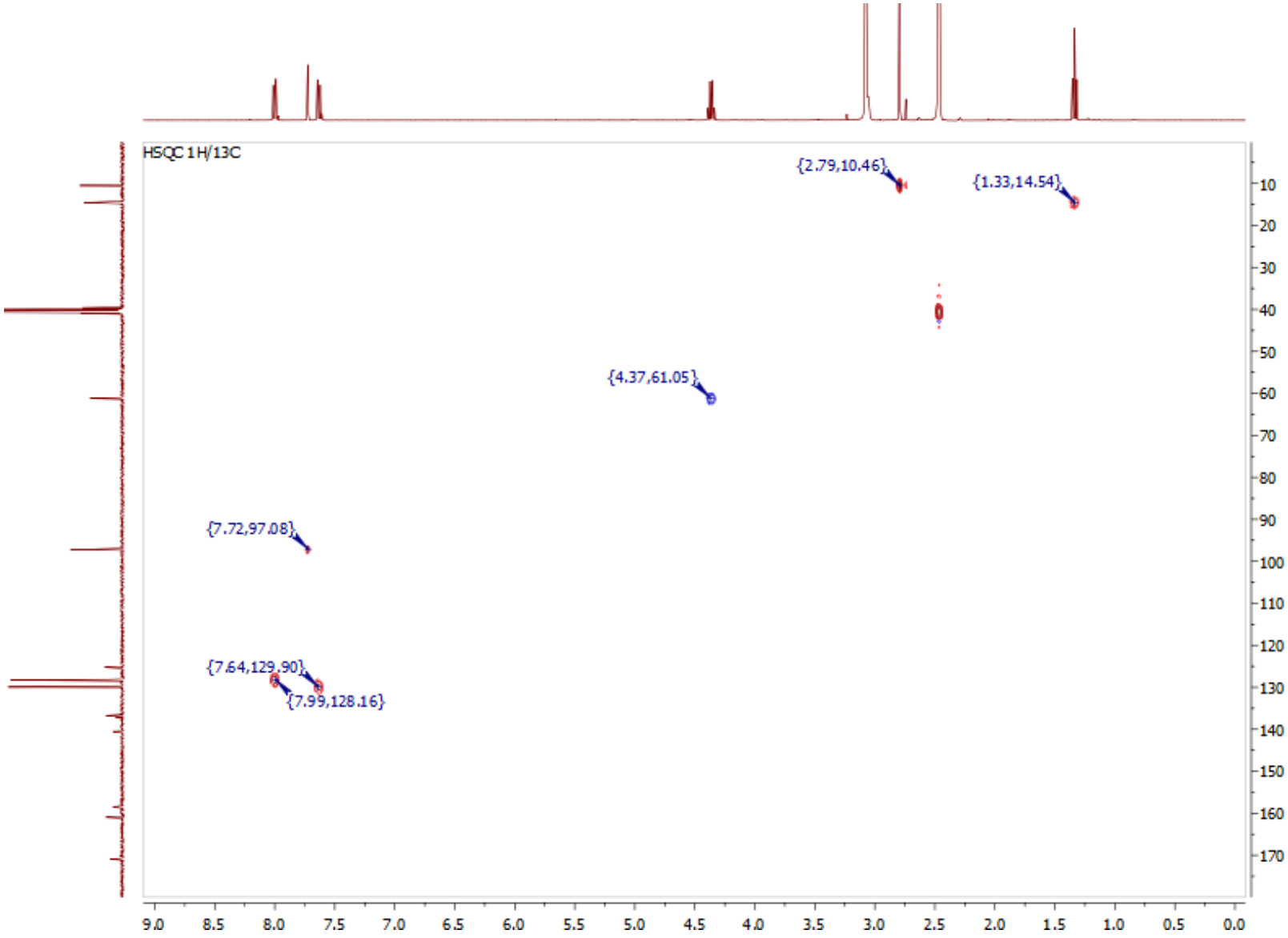


Figure S23. $^{1}H/^{13}C$ HSQC NMR of **4a**

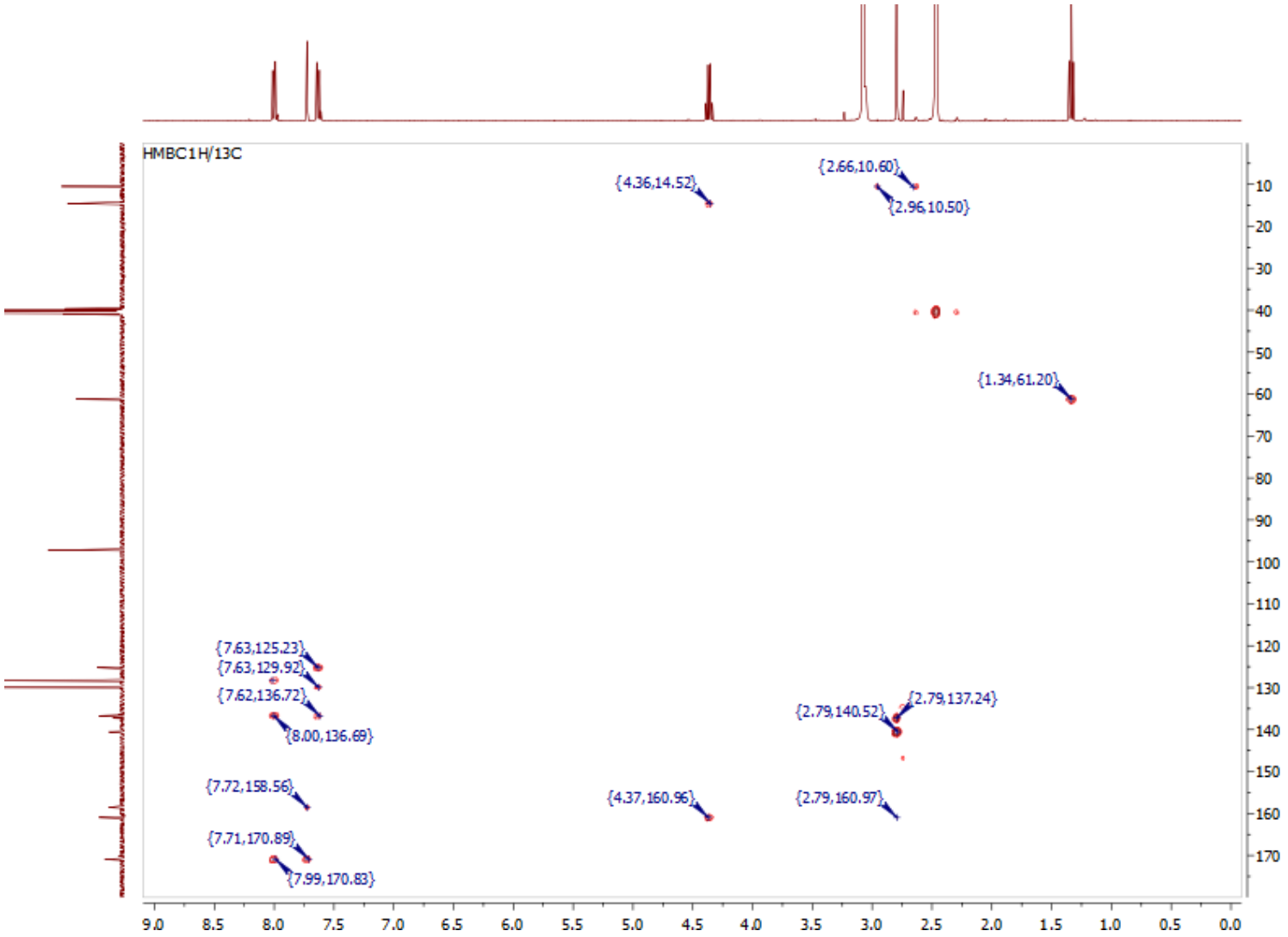


Figure S24. $^{1}H/^{13}C$ HMBC NMR of **4a**

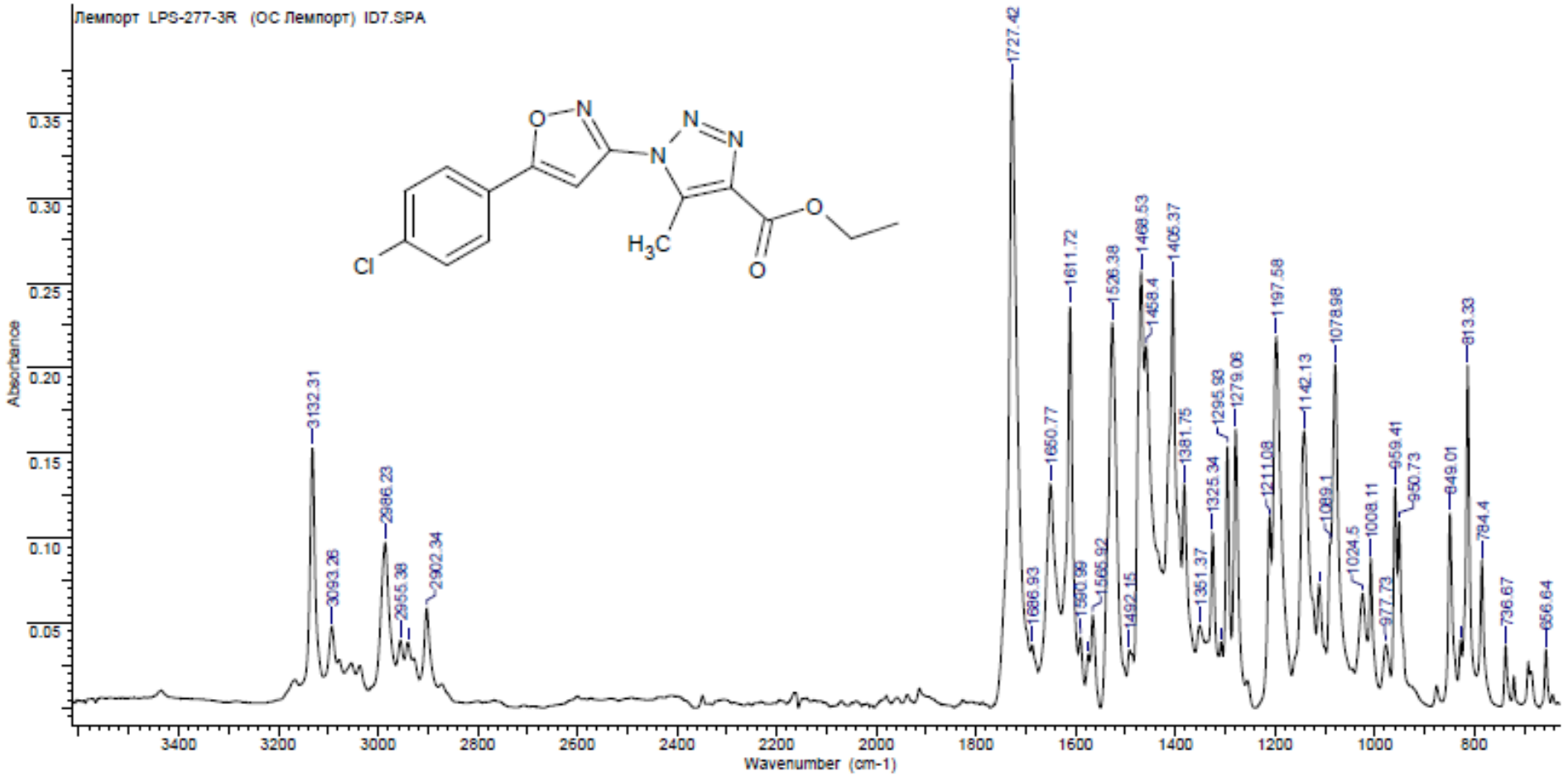


Figure S25. IR-spectrum of **4a**

1-[5-(4-Bromo-phenyl)-isoxazol-3-yl]-5-methyl-1*H*-[1,2,3]triazole-4-carboxylic acid ethyl ester **4b**

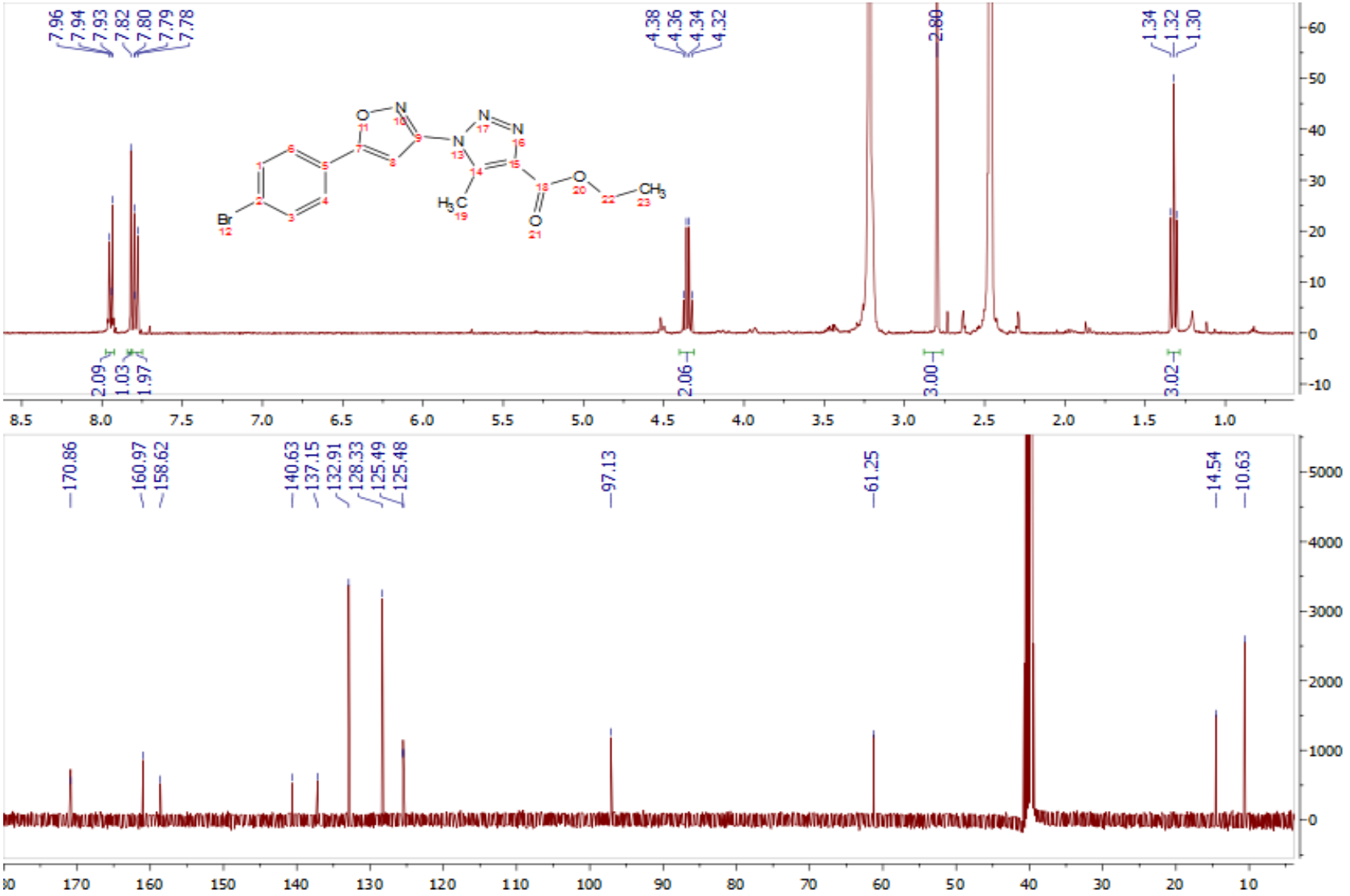


Figure S26. ^{1}H and ^{13}C NMR spectra of **4b** recorded at 60°C

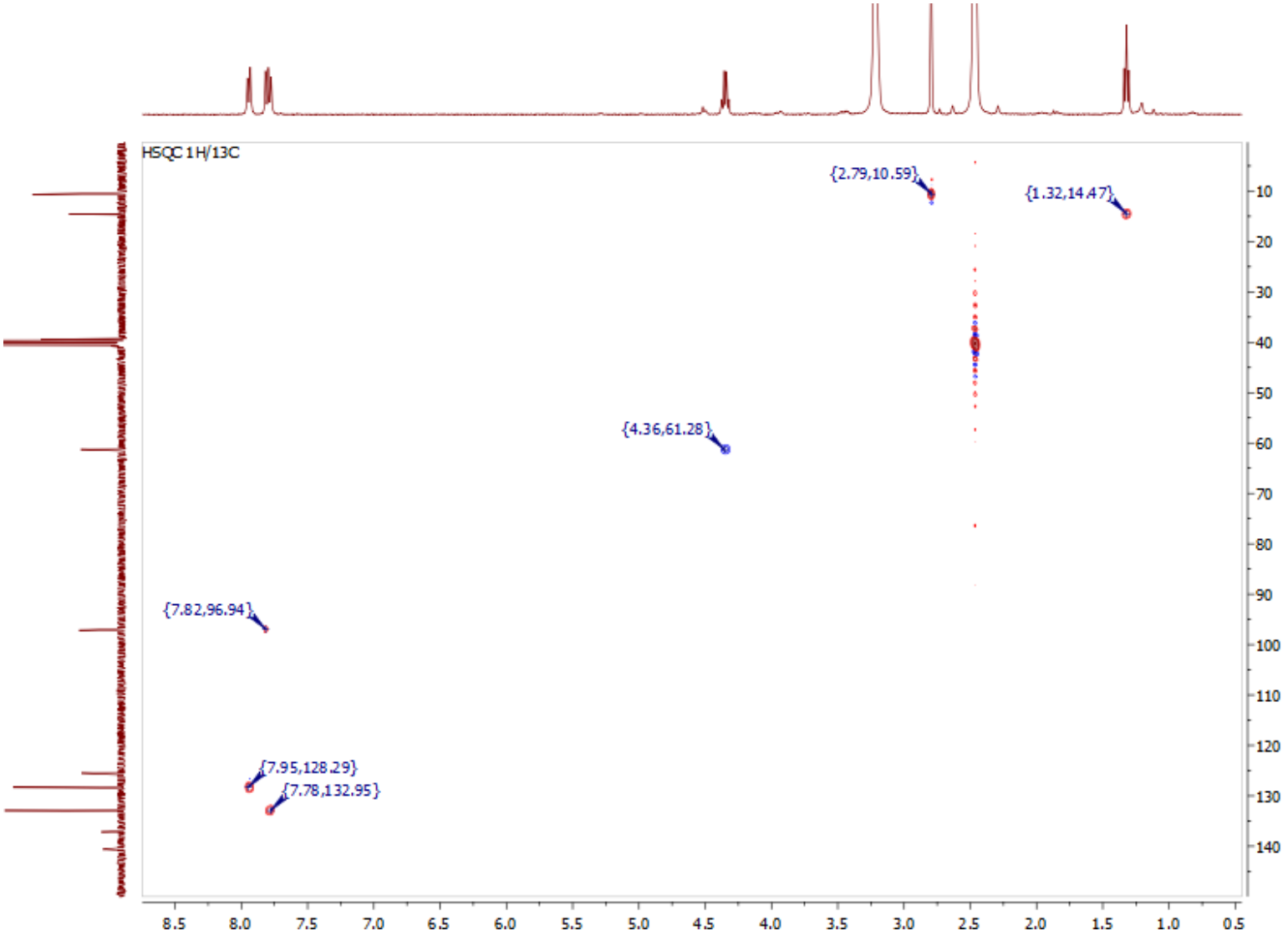


Figure S27. $^{1}H/^{13}C$ HSQC NMR of **4b**

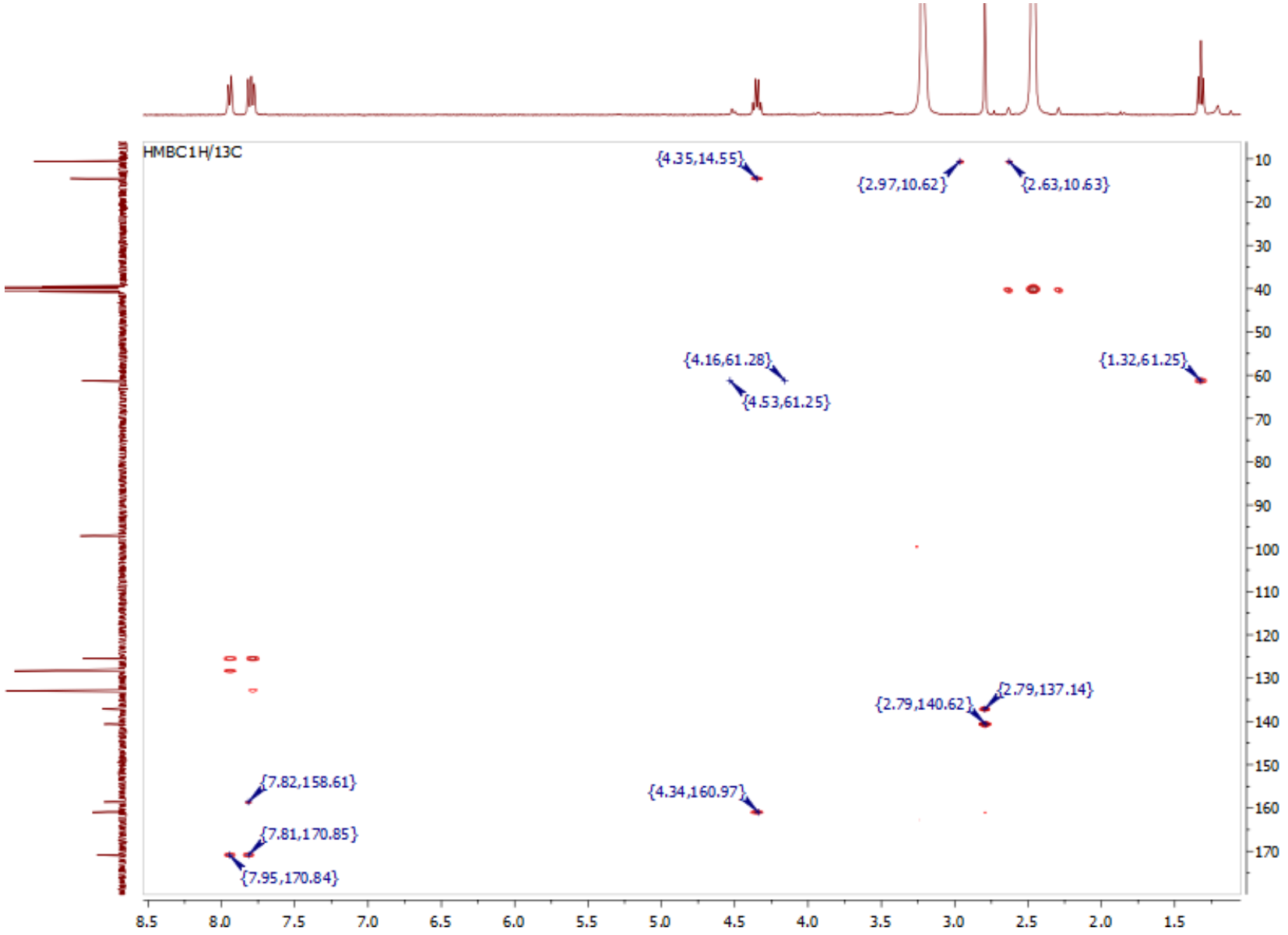


Figure S28. $^{1}H/^{13}C$ HMBC NMR of **4b**

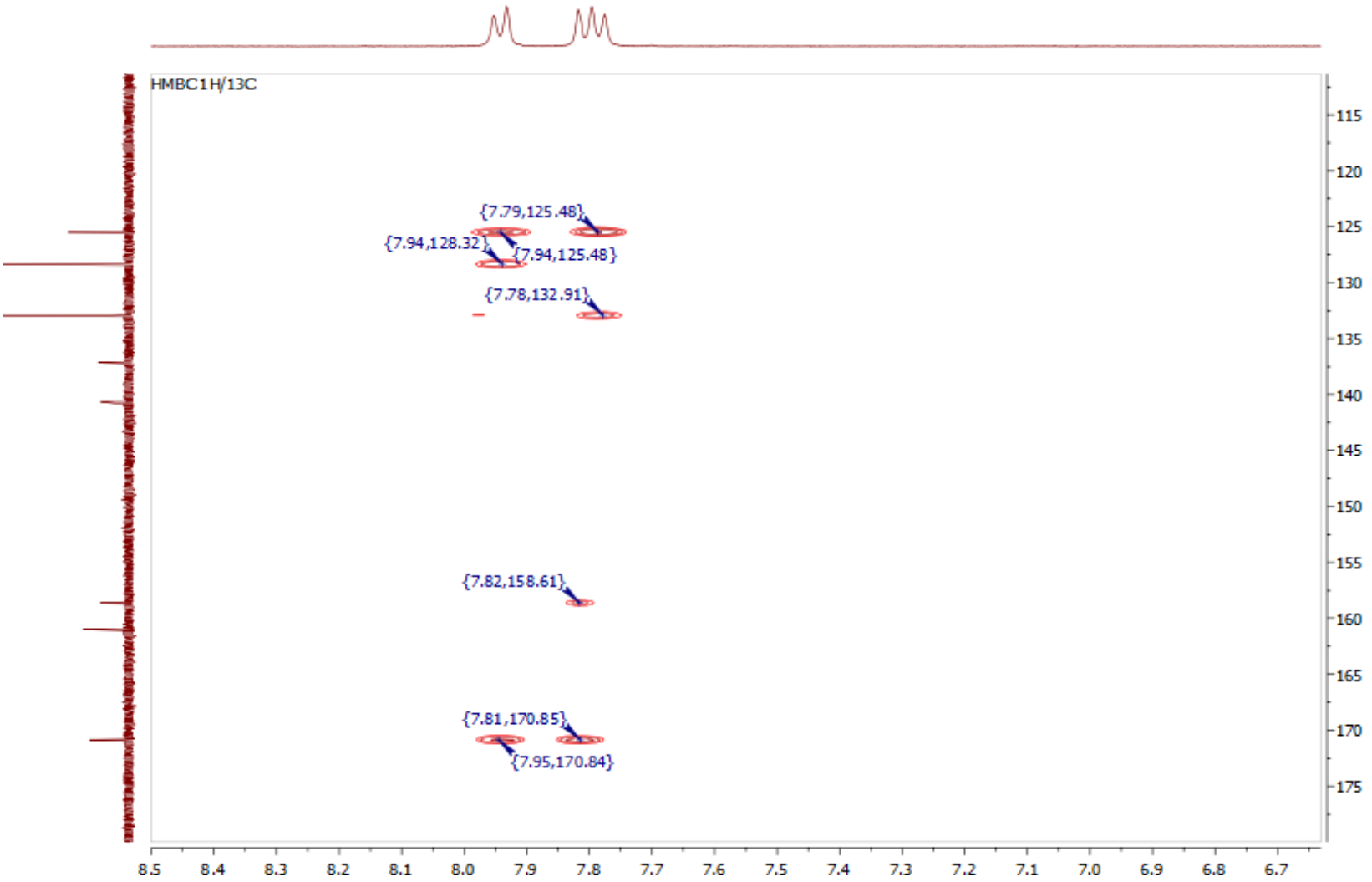


Figure S29. $^{1}H/^{13}C$ HMBC NMR of **4b** (fragment)

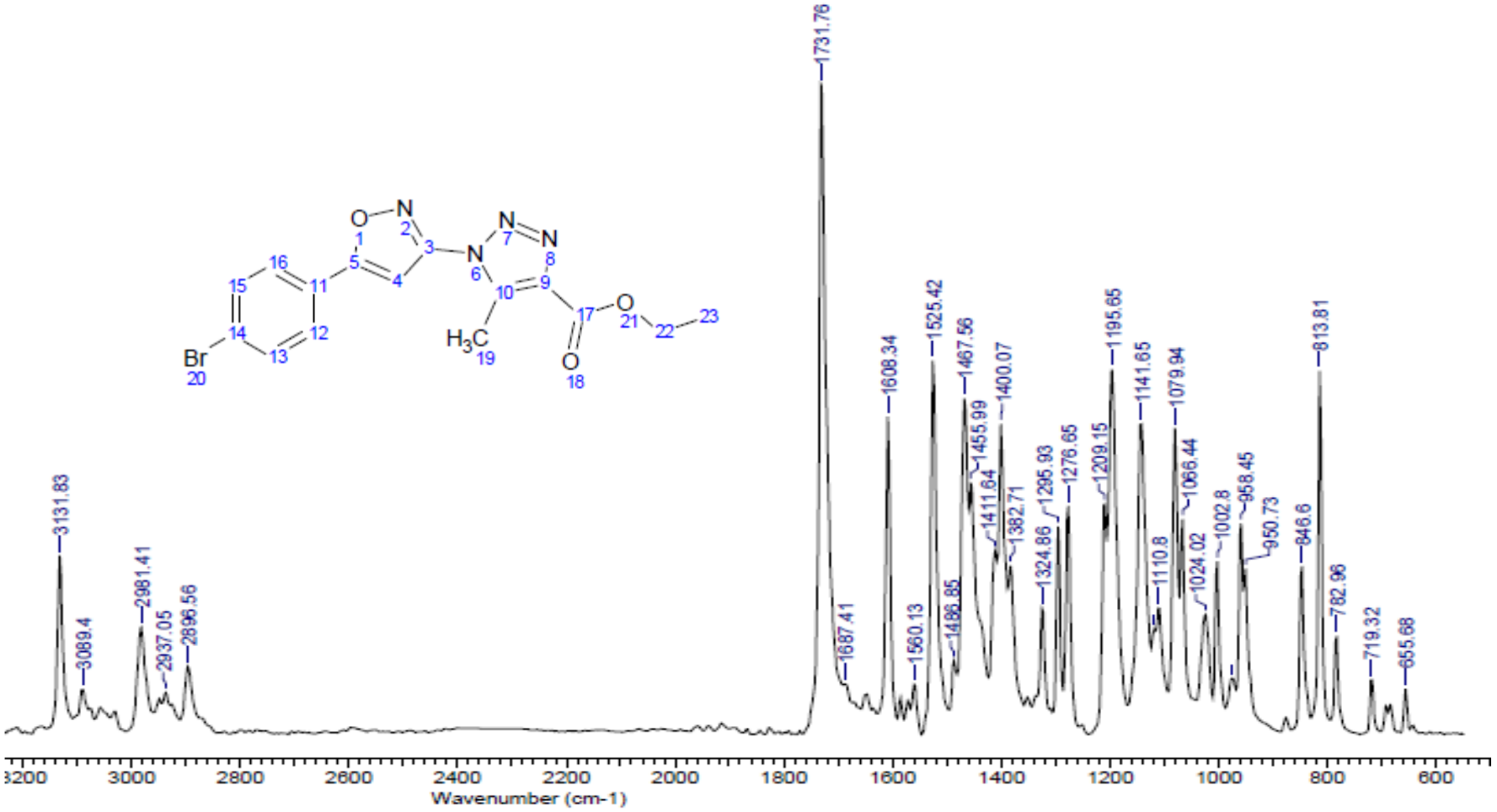


Figure S30. IR-spectrum of **4b**

X-ray structure analysis data

1-[5-(4-Bromo-phenyl)-isoxazol-3-yl]-5-methyl-1*H*-[1,2,3]triazole-4-carboxylic acid ethyl ester **4b**

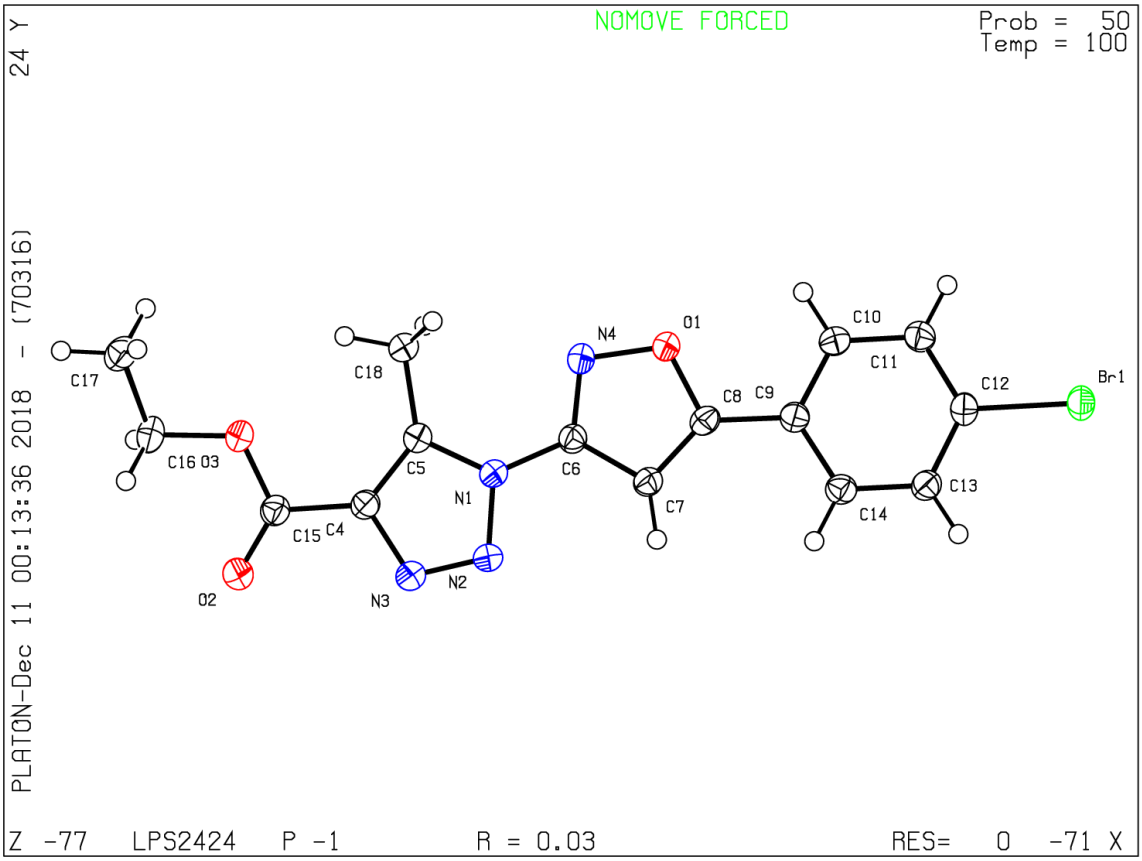


Table S1. Crystal data and structure refinement for **4b**.

Identification code	**4b**	
Empirical formula	C15 H13 Br N4 O3	
Formula weight	377.19	
Temperature	100(2) K	
Wavelength	0.78790 Å	
Crystal system	Triclinic	
Space group	*P*-1	
Unit cell dimensions	a = 6.3358(13) Å	α = 87.49(3)°.
	b = 7.4548(15) Å	β = 87.94(3)°.
	c = 16.165(3) Å	γ = 80.18(3)°.
Volume	751.3(3) $Å^3$	
Z	2	
Density (calculated)	1.667 Mg m^{-3}	
Absorption coefficient	3.545 mm^{-1}	
F(000)	380	
Crystal size	0.15 x 0.10 x 0.03 mm^3	
Theta range for data collection	1.398 to 30.758°.	
Index ranges	-8<=h<=8, -9<=k<=9, -20<=l<=20	
Reflections collected	13210	
Independent reflections	3421 [R(int) = 0.0405]	
Completeness to theta = 28.212°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.900 and 0.610	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3421 / 0 / 211	
Goodness-of-fit on F^2	1.074	
Final R indices [for 3279 rflns with I>2σ(I)]	R1 = 0.0276, wR2 = 0.0725	
R indices (all data)	R1 = 0.0287, wR2 = 0.0732	
Extinction coefficient	0.014(1)	
Largest diff. peak and hole	0.382 and -0.673 e.$Å^{-3}$	

Table S2. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters ($Å^2$ $x10^3$) for **4b**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
Br(1)	8508(1)	-1720(1)	8655(1)	29(1)
O(1)	7165(2)	1790(2)	4716(1)	29(1)
O(2)	-1194(2)	7225(2)	1635(1)	35(1)
O(3)	2257(2)	6563(2)	1208(1)	27(1)
N(1)	3000(2)	4406(2)	3627(1)	23(1)
N(2)	923(2)	5036(2)	3874(1)	26(1)
N(3)	-27(2)	5867(2)	3239(1)	26(1)
N(4)	6315(3)	2686(2)	3992(1)	28(1)
C(4)	1398(3)	5791(2)	2576(1)	24(1)
C(5)	3363(3)	4858(2)	2814(1)	23(1)
C(6)	4352(3)	3391(2)	4213(1)	23(1)
C(7)	3810(3)	3014(2)	5050(1)	24(1)
C(8)	5645(3)	2000(2)	5337(1)	24(1)
C(9)	6312(3)	1126(2)	6133(1)	24(1)
C(10)	8391(3)	152(3)	6212(1)	28(1)
C(11)	9051(3)	-700(2)	6962(1)	28(1)
C(12)	7608(3)	-546(2)	7629(1)	25(1)
C(13)	5546(3)	427(2)	7572(1)	26(1)
C(14)	4892(3)	1260(2)	6818(1)	26(1)
C(15)	645(3)	6607(2)	1771(1)	25(1)
C(16)	1671(3)	7262(3)	382(1)	31(1)
C(17)	3675(3)	7683(3)	-60(1)	34(1)
C(18)	5461(3)	4368(3)	2367(1)	27(1)

Table S3. Bond lengths [Å] and angles [°] for **4b**.

Br(1)-C(12)	1.9003(18)	C(9)-C(14)	1.397(2)
O(1)-C(8)	1.362(2)	C(9)-C(10)	1.399(3)
O(1)-N(4)	1.399(2)	C(10)-C(11)	1.387(3)
O(2)-C(15)	1.202(2)	C(10)-H(10)	0.9500
O(3)-C(15)	1.340(2)	C(11)-C(12)	1.385(2)
O(3)-C(16)	1.450(2)	C(11)-H(11)	0.9500
N(1)-C(5)	1.364(2)	C(12)-C(13)	1.386(3)
N(1)-N(2)	1.371(2)	C(13)-C(14)	1.388(3)
N(1)-C(6)	1.406(2)	C(13)-H(13)	0.9500
N(2)-N(3)	1.290(2)	C(14)-H(14)	0.9500
N(3)-C(4)	1.373(2)	C(16)-C(17)	1.508(3)
N(4)-C(6)	1.308(2)	C(16)-H(16A)	0.9900
C(4)-C(5)	1.378(2)	C(16)-H(16B)	0.9900
C(4)-C(15)	1.471(2)	C(17)-H(17A)	0.9800
C(5)-C(18)	1.487(2)	C(17)-H(17B)	0.9800
C(6)-C(7)	1.412(2)	C(17)-H(17C)	0.9800
C(7)-C(8)	1.359(3)	C(18)-H(18A)	0.9800
C(7)-H(7)	0.9500	C(18)-H(18B)	0.9800
C(8)-C(9)	1.459(2)	C(18)-H(18C)	0.9800

C(8)-O(1)-N(4)	109.38(13)	C(10)-C(11)-H(11)	120.8
C(15)-O(3)-C(16)	116.12(15)	C(11)-C(12)-C(13)	122.32(17)
C(5)-N(1)-N(2)	111.40(14)	C(11)-C(12)-Br(1)	118.35(14)
C(5)-N(1)-C(6)	130.97(15)	C(13)-C(12)-Br(1)	119.33(13)
N(2)-N(1)-C(6)	117.59(14)	C(12)-C(13)-C(14)	118.97(16)
N(3)-N(2)-N(1)	106.92(14)	C(12)-C(13)-H(13)	120.5
N(2)-N(3)-C(4)	109.37(15)	C(14)-C(13)-H(13)	120.5
C(6)-N(4)-O(1)	104.04(14)	C(13)-C(14)-C(9)	120.01(17)
N(3)-C(4)-C(5)	109.36(15)	C(13)-C(14)-H(14)	120.0
N(3)-C(4)-C(15)	118.93(16)	C(9)-C(14)-H(14)	120.0
C(5)-C(4)-C(15)	131.69(16)	O(2)-C(15)-O(3)	124.22(17)
N(1)-C(5)-C(4)	102.95(15)	O(2)-C(15)-C(4)	124.07(16)
N(1)-C(5)-C(18)	124.08(16)	O(3)-C(15)-C(4)	111.71(15)
C(4)-C(5)-C(18)	132.98(16)	O(3)-C(16)-C(17)	107.40(16)
N(4)-C(6)-N(1)	119.67(15)	O(3)-C(16)-H(16A)	110.2
N(4)-C(6)-C(7)	114.03(16)	C(17)-C(16)-H(16A)	110.2
N(1)-C(6)-C(7)	126.30(15)	O(3)-C(16)-H(16B)	110.2
C(8)-C(7)-C(6)	102.96(15)	C(17)-C(16)-H(16B)	110.2
C(8)-C(7)-H(7)	128.5	H(16A)-C(16)-H(16B)	108.5
C(6)-C(7)-H(7)	128.5	C(16)-C(17)-H(17A)	109.5
C(7)-C(8)-O(1)	109.59(15)	C(16)-C(17)-H(17B)	109.5
C(7)-C(8)-C(9)	135.01(16)	H(17A)-C(17)-H(17B)	109.5
O(1)-C(8)-C(9)	115.40(15)	C(16)-C(17)-H(17C)	109.5
C(14)-C(9)-C(10)	119.67(16)	H(17A)-C(17)-H(17C)	109.5
C(14)-C(9)-C(8)	120.52(16)	H(17B)-C(17)-H(17C)	109.5
C(10)-C(9)-C(8)	119.81(16)	C(5)-C(18)-H(18A)	109.5
C(11)-C(10)-C(9)	120.71(16)	C(5)-C(18)-H(18B)	109.5
C(11)-C(10)-H(10)	119.6	H(18A)-C(18)-H(18B)	109.5
C(9)-C(10)-H(10)	119.6	C(5)-C(18)-H(18C)	109.5
C(12)-C(11)-C(10)	118.32(17)	H(18A)-C(18)-H(18C)	109.5
C(12)-C(11)-H(11)	120.8	H(18B)-C(18)-H(18C)	109.5

Table S4. Anisotropic displacement parameters ($Å^2$ x 10^3) for **4b**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	34(1)	28(1)	22(1)	1(1)	-3(1)	-1(1)
O(1)	27(1)	35(1)	21(1)	4(1)	2(1)	3(1)
O(2)	26(1)	47(1)	31(1)	9(1)	-1(1)	-2(1)
O(3)	28(1)	32(1)	21(1)	3(1)	0(1)	-4(1)
N(1)	22(1)	25(1)	21(1)	0(1)	1(1)	-2(1)
N(2)	23(1)	30(1)	24(1)	1(1)	2(1)	-1(1)
N(3)	25(1)	29(1)	24(1)	1(1)	2(1)	-3(1)
N(4)	28(1)	33(1)	21(1)	4(1)	1(1)	1(1)
C(4)	24(1)	24(1)	22(1)	-1(1)	1(1)	-4(1)
C(5)	24(1)	23(1)	22(1)	-1(1)	0(1)	-5(1)
C(6)	24(1)	24(1)	21(1)	-1(1)	-1(1)	-3(1)
C(7)	25(1)	25(1)	22(1)	-1(1)	2(1)	-3(1)
C(8)	26(1)	25(1)	21(1)	-3(1)	3(1)	-4(1)
C(9)	26(1)	23(1)	24(1)	-1(1)	0(1)	-3(1)
C(10)	26(1)	31(1)	25(1)	-1(1)	3(1)	1(1)
C(11)	28(1)	28(1)	26(1)	-1(1)	0(1)	2(1)
C(12)	30(1)	24(1)	21(1)	0(1)	-3(1)	-4(1)
C(13)	27(1)	26(1)	24(1)	-1(1)	2(1)	-4(1)
C(14)	26(1)	23(1)	26(1)	-2(1)	1(1)	-2(1)
C(15)	26(1)	25(1)	24(1)	1(1)	1(1)	-5(1)
C(16)	37(1)	34(1)	21(1)	4(1)	-2(1)	-9(1)
C(17)	38(1)	34(1)	29(1)	2(1)	6(1)	-6(1)
C(18)	25(1)	32(1)	24(1)	1(1)	2(1)	-2(1)

Table S5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for **4b**.

Atom	x	y	z	U(iso)
H(7)	2487	3380	5341	29
H(10)	9361	73	5748	34
H(11)	10458	-1372	7015	34
H(13)	4595	522	8042	31
H(14)	3479	1921	6767	31
H(16A)	577	8378	413	37
H(16B)	1071	6343	82	37
H(17A)	3331	8167	-621	51
H(17B)	4740	6566	-90	51
H(17C)	4256	8588	244	51
H(18A)	6582	4784	2674	41
H(18B)	5384	4954	1812	41
H(18C)	5799	3043	2321	41

Table S6. Torsion angles [°] for **4b**.

C(5)-N(1)-N(2)-N(3)	0.13(19)		
C(6)-N(1)-N(2)-N(3)	-177.97(14)	N(4)-O(1)-C(8)-C(7)	-0.2(2)
N(1)-N(2)-N(3)-C(4)	0.06(19)	N(4)-O(1)-C(8)-C(9)	179.86(14)
C(8)-O(1)-N(4)-C(6)	0.30(19)	C(7)-C(8)-C(9)-C(14)	-0.4(3)
N(2)-N(3)-C(4)-C(5)	-0.2(2)	O(1)-C(8)-C(9)-C(14)	179.55(15)
N(2)-N(3)-C(4)-C(15)	178.13(15)	C(7)-C(8)-C(9)-C(10)	179.8(2)
N(2)-N(1)-C(5)-C(4)	-0.26(18)	O(1)-C(8)-C(9)-C(10)	-0.2(2)
C(6)-N(1)-C(5)-C(4)	177.52(16)	C(14)-C(9)-C(10)-C(11)	0.7(3)
N(2)-N(1)-C(5)-C(18)	179.94(15)	C(8)-C(9)-C(10)-C(11)	-179.51(17)
C(6)-N(1)-C(5)-C(18)	-2.3(3)	C(9)-C(10)-C(11)-C(12)	-0.6(3)
N(3)-C(4)-C(5)-N(1)	0.29(18)	C(10)-C(11)-C(12)-C(13)	-0.1(3)
C(15)-C(4)-C(5)-N(1)	-177.78(17)	C(10)-C(11)-C(12)-Br(1)	179.79(14)
N(3)-C(4)-C(5)-C(18)	-179.94(18)	C(11)-C(12)-C(13)-C(14)	0.8(3)
C(15)-C(4)-C(5)-C(18)	2.0(3)	Br(1)-C(12)-C(13)-C(14)	-179.15(13)
O(1)-N(4)-C(6)-N(1)	-179.93(14)	C(12)-C(13)-C(14)-C(9)	-0.7(3)
O(1)-N(4)-C(6)-C(7)	-0.3(2)	C(10)-C(9)-C(14)-C(13)	-0.1(3)
C(5)-N(1)-C(6)-N(4)	-1.0(3)	C(8)-C(9)-C(14)-C(13)	-179.83(16)
N(2)-N(1)-C(6)-N(4)	176.62(15)	C(16)-O(3)-C(15)-O(2)	-2.2(3)
C(5)-N(1)-C(6)-C(7)	179.40(17)	C(16)-O(3)-C(15)-C(4)	177.36(14)
N(2)-N(1)-C(6)-C(7)	-2.9(2)	N(3)-C(4)-C(15)-O(2)	-5.9(3)
N(4)-C(6)-C(7)-C(8)	0.2(2)	C(5)-C(4)-C(15)-O(2)	172.02(19)
N(1)-C(6)-C(7)-C(8)	179.80(16)	N(3)-C(4)-C(15)-O(3)	174.58(15)
C(6)-C(7)-C(8)-O(1)	-0.01(19)	C(5)-C(4)-C(15)-O(3)	-7.5(3)
C(6)-C(7)-C(8)-C(9)	179.94(19)	C(15)-O(3)-C(16)-C(17)	161.25(16)